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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 12 1959

B.C.G. AND VOLE BACILLUS VACCINES IN THE PREVENTION OF TUBERCULOSIS IN ADOLESCENTS

SECOND REPORT TO THE MEDICAL RESEARCH COUNCIL BY THEIR TUBERCULOSIS VACCINES CLINICAL TRIALS COMMITTEE*

A clinical trial of B.C.G. and vole bacillus vaccines, directed by the Tuberculosis Vaccines Clinical Trials Committee of the Medical Research Council (M.R.C.), was begun in England in 1950, and is still in progress. The effect of the vaccines is being studied during adolescence and early adult life in groups with no special risk of exposure to tuberculous infection, and initially free both from active tuberculosis and from known contact with the disease at home. There are more than 50,000 participants of both sexes in the investigation, all aged 14 to 15½ years on entry, and now aged between 21 and 23 years. Those with negative reactions to tuberculin on entry were vaccinated with B.C.G. or vole bacillus vaccine or left unvaccinated, according to a method of random allocation. All the participants, including those with a positive reaction to tuberculin initially, have now (January, 1959) been followed intensively for more than six years.

The first report of this investigation (M.R.C., 1956; see also Hart, Pollock, and Sutherland, 1957) presented complete results after each participant had been in the trial for two and a half years. The present report gives corresponding results for the period of five years since entry to the trial, together with preliminary incomplete information for the period between five and seven and a half years after entry.

The work described was carried out by the Council's Tuberculosis Research Unit, with the assistance of many statutory and voluntary organizations (see Acknowledgments).

I. PLAN AND CONDUCT OF THE TRIAL

A detailed description of the plan and conduct of the trial was given in the first report (M.R.C., 1956). The following are the main features.

The Intake

The participants in the trial volunteered with their parents' consent between September, 1950, and December, 1952; they were all aged between 14 and 15½ years, and most (82%) were between 14½ and 15 years. All were in their final year at secondary modern schools in densely populated districts in or near North London, Birmingham, and Manchester (see Acknowledgments). A record card bearing a printed serial number was prepared for each volunteer, who was then given the following standard examination by one of three special teams of the Tuberculosis Research Unit, each operating in one of the main areas: (*a*) A 35-mm. radiograph of the chest; and, if indicated, a full-plate radiograph. (*b*) An intracutaneous tuberculin (Mantoux) test with 3 T.U. (tuberculin units) of Old Tuberculin (human). (*c*) If there was no palpable infiltration, or if its greatest diameter was less than 5 mm. at the end of 72 hours, the reaction to 3 T.U. was regarded as negative and another test was made with 100 T.U.

Participants with no infiltration, or with a diameter of infiltration of less than 5 mm., in response to the second test, at the end of 72 hours, were regarded as negative reactors to 100 T.U. and were eligible for vaccination.

*Members of the Committee: Dr. P. D'Arcy Hart (chairman), Dr. C. Metcalfe Brown, Sir John Charles, Professor R. Cruickshank, Dr. Marc Daniels (secretary until his death in 1953), Dr. W. Pointon Dick (resigned in 1951), Dr. J. E. Geddes, Professor A. Bradford Hill, Sir Wilson Jameson, Dr. V. H. Springett, Dr. Ian Sutherland, Dr. A. Q. Wells (died in 1956), Dr. G. S. Wilson, Dr. T. M. Pollock (secretary)

Vaccination Procedures

The children eligible for vaccination were allocated, according to the final digit of the serial number on their record card, to the unvaccinated group, or to one of the two vaccinated groups. B.C.G. vaccine was given in all three areas, but vole bacillus vaccine was not given in the London area. On a few occasions in the Birmingham and Manchester areas, when there was a temporary failure in the supply of one of the vaccines, the other was used instead. Because of these local differences the numbers of participants in the unvaccinated groups and in the two vaccinated groups were unequal. Throughout the trial, however, and whatever vaccines were being given, the allocation was always strictly in accordance with the final digit of the serial number, and so was effectively random.

The B.C.G. vaccine used was the fresh liquid preparation from the State Serum Institute, Copenhagen, and was given by intracutaneous injection. In the course of the trial 75 of the Institute's routine batches were used. The viable units/mg. for each batch (Tolderlund, 1952, 1955) ranged from 7.8 to 53.4m., and 74% of the participants given B.C.G. were vaccinated with batches which had counts between 20 and 40m. viable units/mg. The vole bacillus vaccine was a fresh liquid preparation from the Lister Institute, Elstree, Herts, and was given by multiple puncture. The earlier batches of this vaccine were below the strength originally intended. Further details of both vaccines, and of the vaccination procedures, are given in the first report (M.R.C., 1956); the tuberculin conversion rates are given below in Table II.

The appropriate vaccine was given immediately after the reading of the test with 100 T.U.

Number of Participants in the Trial

In this report the numbers of participants in the trial have been estimated from the same representative

samples of the record cards as were used in the first report. The cases of tuberculosis and other diseases, however, have, as before, been completely enumerated. (In the final report the analysis will be based on a complete enumeration of the participants also; in the meantime, however, checks have shown that any inaccuracies in the numbers of participants, as estimated from the samples, will not affect the final rates appreciably.)

The following groups of children were excluded from participation: (*a*) Those found or suspected to have any form of tuberculosis (apart from calcification of primary type) at the time of the first examination. (*b*) Those, who, at the time of the first examination, had been in recent contact at home with a case of pulmonary tuberculosis. (*c*) Those who failed to complete the first examination.

In addition, a small number (about 400) have been excluded from the analysis of the results for such reasons as having been given the wrong vaccine, incorrectly left unvaccinated, or given a tuberculosis vaccine prior to entering the trial. After these exclusions there remain 56,700 participants in the analysis.

As a result of the tuberculin tests and vaccinations at the first examination, the children were automatically classified on entry into the following five trial groups, in which they remain for the purpose of the ensuing analysis, whatever the results of subsequent tuberculin tests:

Negative unvaccinated.—Negative to 100 T.U. on entry and left unvaccinated: 13,300 participants.

Negative, B.C.G.-vaccinated.—Negative to 100 T.U. on entry and then given B.C.G. vaccine: 14,100 participants.

Negative, vole-bacillus-vaccinated.—Negative to 100 T.U. on entry and then given vole bacillus vaccine: 6,700 participants.

Positive to 3 T.U.—Positive to 3 T.U. on entry and left unvaccinated: 16,000 participants.

Positive only to 100 T.U.—Negative to 3 T.U. but positive to 100 T.U. on entry, and left unvaccinated: 6,600 participants.

Second Examination of Participants

In 1950 and 1951, the children in the trial had another chest radiograph before leaving school, usually three to five months after the first examination; those with negative reactions to 100 T.U. at the first examination, whether vaccinated or not, were retested as before. At the same time the B.C.G.- and vole-bacillus-vaccination reactions were examined. In 1952, to check the potency of the vaccines, a sample of the children given each batch had tuberculin tests performed, and vaccination reactions examined, three to five months after vaccination.

Follow-up of Participants

Since leaving school the participants in each of the five trial groups have had the following cycle of inquiry and examination, repeated at intervals of about 14 months: (*a*) An inquiry form by post about four months after leaving school (or after the previous chest radiograph). (*b*) A home visit by a trained nurse about six months after the postal inquiry. (*c*) The three teams have visited each district in turn about four months after the home visit, to take chest radiographs and make tuberculin tests, exactly as at the first examination at school (except that some of the tuberculin tests were read at 48 instead of 72 hours); participants who failed to attend this examination were invited again to a special examination about seven months later. Since June, 1954, all the radiographs have been read separately by a physician unconnected with the conduct of the trial as well as by the team physician.

The great majority of the participants have continued to live in their original areas, and only about 6% have moved to a district (either in this country or abroad) not visited by the teams' mobile radiography units. For these participants the home visits and the radiographic examinations were arranged by the local health authority.

Arrangements were made with the medical services of the Royal Navy, the Army, and the Royal Air Force for the close follow-up of participants during their two-year period of military service. This has involved about two-thirds of the young men, mostly between the ages of 18 and 20 years. The Army and the Royal Air Force introduced a special scheme for the prompt notification to the M.R.C. teams of any case of tuberculosis which developed in a trial participant, and arranged, where practicable, for chest radiographs and (in the Royal Air Force) tuberculin tests on demobilization. The Royal Navy made available a nominal roll of those invalided with tuberculosis. During this period of military service the M.R.C. teams also made a single postal inquiry to the participant's home.

In addition, where it was known that a participant had attended one of the mass miniature radiography units of the National Health Service, or had had any other routine chest radiograph (for example, at an antenatal clinic), efforts were made to ascertain the result.

Recent analysis of a sample of the records (for all whose surnames began with A or D, representing 6.5% of the total) has shown that contact was made by one or more of these means with 89% of the participants during the two-year period 1957–8, compared with 94% within the first 18 months after entry to the trial (M.R.C., 1956). Sixty per cent. of the participants had at least one chest radiograph taken in 1957–8, compared with at least 74% within the first two years after entry.

Information has also been continually made available to the teams from the tuberculosis notification registers of the medical officers of health and from the records of attendances at the chest clinics and mass radiography units of the National Health Service, in the districts concerned. Cases of tuberculosis have therefore come to the notice of the M.R.C. teams through the usual channels of the National Health Service (56% of the cases within five years of entry) as well as by their own radiographic examinations (44%). Throughout this report, the small number of cases arising among participants during their period of service in the armed forces have been included with the National Health Service cases.

Vaccination of Trial Participants from Outside Sources

No participant was vaccinated or revaccinated by the M.R.C. teams subsequent to the initial examination, and there was little opportunity for participants to receive B.C.G. vaccine from outside sources during the course of the trial. Those known to be in contact at home with pulmonary tuberculosis at the time of entry were

excluded from participation, and the current national scheme for the vaccination of 13-year-old school children (Ministry of Health, 1953) did not begin until all the participants were aged at least 16 years. Some participants, however, have come into contact with tuberculosis at home since entry, and some have had an opportunity for vaccination in their occupation (for example, nursing) or in other ways.

Information on such vaccination has been made available to the teams at frequent intervals from the vaccination records of the chest physicians and medical officers of health in the districts concerned. In addition, any participant in the negative unvaccinated group who has become tuberculin-positive since September, 1955, has been routinely questioned about possible vaccination from outside sources, and the arm has been examined for a vaccination reaction. As a result of these inquiries and other information, it has been found that very few participants have been given B.C.G. vaccine from outside sources. A recent survey of a sample of the records has shown only four instances of non-trial B.C.G. vaccination in a total of about 2,500 participants from all trial groups (1.6 per 1,000). Two were initially in the tuberculin-negative unvaccinated group and one was in each of the two vaccinated groups. It is evident that the present extent of non-trial vaccination of participants can have had only a negligible influence on the results.

Records of Cases

The physicians in charge of the M.R.C. teams were not responsible for the further investigation or treatment of any participant who had an abnormal radiograph; those found to have an abnormal radiograph at an examination by one of the teams were referred to their local chest clinics. However, almost every case of definite or suspected tuberculosis brought to the notice of the teams was also examined by one of the team physicians, and further details of progress were obtained at regular intervals. To ensure that cases of tuberculosis were not missed, full records were kept, not only for the definite cases, but also for those in which tuberculosis was either suspected or considered to be even a possible diagnosis. Similar records were kept for all non-tuberculous pulmonary lesions which came to the notice of the teams. As a precaution, it was decided in November, 1953 (with retrospective application), that any pulmonary radiographic abnormality, whatever its apparent cause, which persisted for longer than 14 days without complete clearing must be investigated. Details were obtained of all deaths, from whatever cause.

In cases of definite or suspected tuberculosis arising in B.C.G.-vaccinated or vole-bacillus-vaccinated participants, routine examinations of cultures growing acid-fast bacilli were made to investigate whether the organisms were B.C.G. or vole bacilli.

Assessment of Cases

All definite, suspected, and possible cases of tuberculosis, and all other pulmonary radiographic abnormalities persisting for longer than 14 days, which came to the notice of the teams were reviewed by an independent assessor who was kept unaware of the results of any tuberculin tests and whether any vaccination had been performed. The great majority of the cases were reviewed by one assessor, but a second was used for a small number of cases which happened to be under the routine clinical care of the first; and a few cases of suspected tuberculosis of bones or joints, without bacteriological or histological confirmation, were referred to a third.

The assessor decided, from the periodic radiographs, from the results of the clinical examination by one of the team physicians, from the results of clinical examinations by other physicians, and from the results of any bacteriological or pathological examinations: (*a*) whether the disease was definite (and active) tuberculosis, possible tuberculosis, or not tuberculosis; for a few cases he decided that there was no evidence of any disease, tuberculous or non-tuberculous; (*b*) for cases of definite or possible tuberculosis, the form of the disease and the character, course, initial, and maximal extent of any lesions apparent on the series of radiographs; (*c*) for pulmonary lesions, the date of the first abnormal radiograph, or, for other lesions, the date when the first definite symptoms or signs were observed (irrespective of when the diagnosis of tuberculosis had been made); this date has been regarded as the starting-point of the illness, though it will be appreciated that for some cases the starting-point, thus defined, may be a considerable time after the true, but unknown, date of onset of the disease.

II. THE CASES OF TUBERCULOSIS

Cases of Tuberculosis Present on Entry to the Trial

As described in the first report (M.R.C., 1956), 70 cases of previously unsuspected definite tuberculosis were discovered at the first examination at school, and so were excluded from the trial. In addition (up to the end of January, 1959) 111 cases, discovered after the 56,700 participants had completed the first examination and had entered the trial, were judged by the assessor to have started before entry (all except seven were, unknown to the assessor, tuberculin positive on entry). Of these, 80 were cases of definite but previously unsuspected tuberculosis, 18 were definite cases with a history of tuberculosis prior to entry to the trial (unknown to the teams at the time of the first examination), and 13 were cases of possible tuberculosis. These 111 children should also have been excluded from the trial, and have therefore been excluded from the analysis.

In 86 of the 111 cases the radiograph taken on entry showed, on re-scrutiny, abnormal appearances indicative of tuberculosis; in one case with a normal 35-mm. radiograph on entry there had been a pleural effusion two months earlier, and in 19 cases of non-pulmonary disease symptoms had been present before the participant entered the trial. There remain five cases of definite tuberculosis where the assessor decided that the disease must have been present at the time of entry, although the symptoms or lesions were not apparent until later. In one of the five, symptoms of non-pulmonary disease appeared only three months after the child had entered the trial. In the other four, pulmonary lesions were first seen on radiographs taken at the second examination at school; the 35-mm. radiograph on entry in one case was considered not to be of sufficiently high quality to exclude the presence of the lesion, and in two others the film had been lost; in the fourth case the assessor considered that the lesion

was probably present on entry but was obscured by bony shadow. These five children had (unknown to the assessor) all given a positive reaction to tuberculin on entry to the trial.

Tuberculous Lesions Attributed to Vaccination

In seven participants, lesions which developed subsequent to B.C.G. or vole bacillus vaccination were brought to the attention of the teams as cases of tuberculosis and submitted to the assessor, but were regarded by him as complications of vaccination. There were three cases of erythema nodosum, all observed one month after entry to the trial. There were also four cases of regional tuberculous adenitis (one cervical, two axillary, and one inguinal) observed three, six, eight, and 22 months respectively after entry to the trial. In the course of his assessment, the assessor suggested that if the participant had been vaccinated the lesions could have been due to the vaccinating organism. For these cases, and for no others, the assessor was then informed that the participant had been vaccinated. As a result, he attributed all seven cases to the vaccinating organism. The three cases of erythema nodosum occurred in B.C.G.-vaccinated participants, and the four cases of tuberculous adenitis in vole-bacillus-vaccinated participants (all of whom were given the vaccine after it had been brought up to standard—see "Vaccination Procedures," p. 379).

In addition, as described in the first report (M.R.C., 1956), examinations of the vole-bacillus-vaccination sites during the follow-up revealed occasional lesions indistinguishable from lupus vulgaris, at or around the site of vaccination. All occurred among the 4,200 participants given the vaccine after it had been brought up to standard. Of these cases, 23 severe enough to require treatment were found up to the end of January, 1959; all had been referred for treatment before July, 1955. A recent inquiry has shown that in 17 of these 23 cases the lesions had healed; three cases had made a satisfactory early response to treatment, but have not been seen recently; and three failed to attend for treatment or subsequent observation. The B.C.G.-vaccination sites were also examined as a routine, but no similar lesions were found.

All these lesions have been regarded as complications of vaccination, and none of the cases has been included in the tables which follow (but see Discussion, p. 391). It should be emphasized that there was no evidence that any of the other cases of tuberculosis in vaccinated participants were due to the vaccinating organism (see "Bacteriological and Pathological Investigations," p. 386).

Death from Tuberculosis in the First Five Years

Only one participant is known to have died of tuberculosis within five years of entry to the trial. The participant was in the tuberculin-negative unvaccinated

TABLE I.—*Cases of Tuberculosis Starting Within Five Years of Entry to the Trial*

Section*		Trial Group	Estimated No. of Participants	Definite Cases of Tuberculosis		Possible Cases of Tuberculosis Starting Within 5 Years
				No. Starting Within 5 Years	Annual Incidence per 1,000 Participants	
A	Children admitted concurrently with those given B.C.G. vaccine	Negative unvaccinated	13,200	151	2·29	9
		Negative, B.C.G. vaccinated	14,100	27	0·38	3
		Positive to 3 T.U.	15,800	127	1·61	6
		Positive only to 100 T.U.	6,500	30	0·92	3
B	Children admitted concurrently with those given vole bacillus vaccine	Negative unvaccinated	6,500	85	2·62	7
		Negative, vole bacillus vaccinated	6,700	11	0·33	2
		Positive to 3 T.U.	8,800	76	1·73	3
		Positive only to 100 T.U.	3,600	17	0·94	2
C	Children admitted concurrently with those given B.C.G. and those given vole bacillus vaccine	Negative, B.C.G. vaccinated	6,400	10	0·31	2
		Negative, vole bacillus vaccinated	6,400	8	0·25	2

* Many participants and cases of tuberculosis appear in more than one of the three separate sections of this table (see text), and the figures from different sections can therefore not be totalled. The total numbers of participants and cases of tuberculosis in each trial group are shown in Table VIII.

TABLE II.—*Conversion Rates and Incidence of Tuberculosis in Participants Given Different Batches of the B.C.G. and the Vole Bacillus Vaccines*

Classification of Vaccine Batches			Conversion Rates (Estimated from Sample)				Incidence of Tuberculosis		
			No. Who Completed Skin Tests 3 to 5 Months After Vaccination	Percentages with Positive Tuberculin Reactions			Total Participants Given These Batches (Estimated from Sample)	Definite Cases of Tuberculosis Starting Within 5 Years	Annual Incidence per 1,000 Participants
				Positive to 3 T.U.	Positive Only to 100 T.U.	Total Positive			
B.C.G. Vaccine	Viable Units (million) per mg.	Under 20	1,200	*76*	*24*	*100*	1,900	4	0·42
		20–	2,200	*82*	*17*	*99*	4,300	12	0·56
		30–	3,000	*89*	*11*	*100*	6,200	7	0·23
		40 or more	800	*97*	*3*	*100*	1,500	4	0·53
		All batches*	7,200	*86*	*14*	*100*	13,900	27	0·39
Vole Bacillus Vaccine	Concentration of Bacilli and Strain	Substandard† (Jan., 1951 July, 1951)	1,800	*31*	*56*	*87*	2,500	5	0·40
		Standard (Sept., 1951 Dec., 1952)	2,000	*88*	*12*	*100*	4,200	6	0·29
		All batches	3,800	*61*	*33*	*94*	6,700	11	0·33

* Excluding one batch of B.C.G. vaccine, given to about 200 participants, for which no viable count was available.
† That is, below the standard originally intended.

group, and died from acute tuberculous meningitis 39 months after entry.

Incidence of Tuberculosis in the First Five Years

By the end of June, 1958, every participant had been in the trial for five years, and some for as long as seven and a half years. The great majority of the cases of tuberculosis starting within five years of entry are therefore presumed to have come by now (January, 1959) to the notice of the teams. A total of 349 cases of definite tuberculosis started within five years of entry (including the above fatal case) and a further 23 were assessed as possible tuberculosis. Of the definite cases, 153 occurred in the negative unvaccinated group, 27 in the B.C.G.-vaccinated group, 11 in the vole-bacillus-vaccinated group, 128 among those initially positive to 3 T.U., and 30 among those initially positive only to 100 T.U.

A valid assessment of the value of B.C.G. vaccination must be based upon those children who were admitted *concurrently* to the negative unvaccinated, the B.C.G.-vaccinated, and the two tuberculin-positive groups. The data are presented in this way in Section A of Table I. (The comparison includes all the children admitted to the trial in these four groups, except for the small number who entered when vole bacillus vaccine only was available.) In this comparison there were 151 cases of tuberculosis in the tuberculin-negative unvaccinated group, giving an annual incidence of 2.29 cases per 1,000 participants. With its 27 cases, the annual incidence in the B.C.G.-vaccinated group was much lower, being 0.38 per 1,000, or approximately one-sixth of the rate in the negative unvaccinated group. The possibility of this difference having occurred by chance is remote (less than one in a million). Among those initially positive to 3 T.U. the annual incidence was 1.61 per 1,000, rather less than that in the negative unvaccinated group, while in the group positive only to 100 T.U. it was much less, namely 0.92 per 1,000; the latter rate was, however, higher than the rate in the B.C.G.-vaccinated group. These four rates all differ significantly from each other at the 1% level. The variations in incidence *within* the group initially positive to 3 T.U., noted in the first report (M.R.C., 1956), are considered in detail below (see "Incidence of Tuberculosis in Different Periods," p. 387).

Similarly, a valid assessment of the value of vole bacillus vaccination must be based upon those children admitted *concurrently* to the negative unvaccinated, the vole-bacillus-vaccinated, and the two tuberculin-positive groups, as shown in Section B of Table I. (This comparison therefore includes some but not all of the children considered in Section A above, together with the small number who entered the trial at a time when vole bacillus vaccine only was available.) In this comparison there were 85 cases of tuberculosis in the negative unvaccinated group, giving an annual incidence of 2.62 per 1,000; in the vole-bacillus-vaccinated group there were 11 cases, giving a rate of 0.33 per 1,000, or approximately one-eighth of the rate in the negative unvaccinated group. The possibility of this difference having occurred by chance is remote (less than one in a million). Among those initially positive to 3 T.U. the annual incidence was 1.73 per 1,000, rather less than that in the negative unvaccinated group, while in the group positive only to 100 T.U. it was much less, namely 0.94 per 1,000; the latter rate was, however, higher than that in the vole-bacillus-vaccinated group. These four rates all differ significantly from each other at the 1% level (apart from the rates in the two initially positive groups, which differ from each other at the 5% level).

Finally, a valid comparison between the value of B.C.G. and vole bacillus vaccination must also be based on concurrent admissions to these two groups; the data for this comparison are shown in Section C of Table I. (These participants are all included either in Section A or in Section B.) The difference between the annual rates for the B.C.G.-vaccinated group (0.31 per 1,000) and for the concurrent group of vole-bacillus-vaccinated children (0.25 per 1,000) does not attain statistical significance.

The 23 cases judged by the assessor to be possibly but not definitely due to tuberculosis are also shown in Table I; their distribution among the five trial groups is similar to that of the definite cases. The above comparisons would not have been appreciably affected if these possible cases had been included with the definite cases.

Although it is essential for valid comparisons between the trial groups to base them upon concurrent admissions, it is also evident from Table I that the incidence of tuberculosis in each trial group is closely similar in the different sections of the table. In fact, when allowance is made for the overlap between the sections, none of these differences in incidence attains statistical significance. Because of this homogeneity of the findings, it is unnecessary to set out all the results on a strictly concurrent basis. For most of this report, therefore, the findings are presented for the *whole* of each trial group.

Incidence of Tuberculosis in Participants Given Different Batches of B.C.G. Vaccine

Counts of viable bacilli were made as a routine on each weekly batch of B.C.G. vaccine at the State Serum Institute, Copenhagen, prior to dispatch to Britain. These counts were available for all except one of the 75 batches used in the trial (Tolderlund, 1952, 1955). It was thus possible to investigate whether the tuberculin conversion rate, or the incidence of tuberculosis, following vaccination, was associated with routine fluctuation in the strength of the vaccine. The batches were divided into four groups, according to viable count (Table II).

The total proportion converted (based on representative samples) was practically 100% for each group of batches; but there was a definite trend in the proportion converted to 3 T.U. with increasing viable count, from 76% for the batches with a count of less than 20m. viable units/mg. to 97% for those with a count of 40m. or more.

Despite the trend in percentage converted to 3 T.U., there was no obvious trend in the incidence of tuberculosis following vaccination with the different groups of batches. In particular, it is of value to note that the weakest batches in the range used conferred substantial protection against the disease. Of the 12 batches with counts of less than 20m. viable units/mg., 11 had counts between 19.2 and 11.4m., and one had a count of 7.8m. Four cases of tuberculosis started within five years of entry among the 1,900 participants vaccinated with these 12 batches, giving an annual incidence of 0.42 per 1,000. This was considerably less

than the annual rate of 2.00 per 1,000 for the 18 cases occurring in the 1,800 concurrent admissions to the negative unvaccinated group (not shown in Table II); the difference is significant at the 1% level.

Incidence of Tuberculosis in Participants Given Certain Batches of Vole Bacillus Vaccine

As described in the first report, the early batches of vole bacillus vaccine, used from January to July, 1951, were weaker than the standard originally intended, and the strength of the subsequent batches was adjusted to the intended standard. The findings on tuberculin conversion and subsequent incidence of tuberculosis in participants given these two groups of batches are shown in the lower part of Table II.

For the early batches the proportion converted to 3 T.U. was 31%, and the total proportion converted was 87%; for the later batches the corresponding proportions were 88% and 100%.

Despite this considerable difference in the degree of sensitivity produced by the two groups of batches, the incidence of tuberculosis in the participants given the early vaccine was not substantially different from that in the participants given the late vaccine. These early batches, despite the low conversion rate, thus afforded considerable protection against the disease. Five cases of tuberculosis started within five years of entry among the 2,500 participants vaccinated with the early batches, giving an annual incidence of 0.40 per 1,000, compared with 35 cases among the 2,300 concurrent admissions to the negative unvaccinated group, an annual incidence of 3.04 per 1,000 (not shown in Table II). The difference between the rates is significant at the 0.1% level.

Evidence of Vaccination in Cases of Tuberculosis Occurring in Vaccinated Participants

Evidence that the vaccination was technically satisfactory for the 38 definite cases of tuberculosis in the two vaccinated groups is summarized in Table III.

TABLE III.—*Evidence of Technically Satisfactory Vaccination in the 38 Vaccinated Participants who Developed Definite Tuberculosis Within Five Years of Entry to the Trial*

Results of First Skin Test After Vaccination and Before Starting-point of Disease		Vaccination Reaction			
		Total	Present	Absent	Not Examined
Tests within 6 months of vaccination*	Positive to 3 T.U.	18	14	2	2
	Positive only to 100 T.U.	3	2	1	0
	Negative to 100 T.U.	0	0	0	0
Tests 6 months or more after vaccination*	Positive to 3 T.U.	4	4	0	0
	Positive only to 100 T.U.	1	0	1	0
	Negative to 100 T.U.	0	0	0	0
No test		12	10	1	1
All cases		38	30	5	3

* Of the total of 26 vaccinated participants known to have become tuberculin positive, 24 had a normal chest radiograph at the same time or subsequently; two had no chest radiographs taken after vaccination and before the starting-point of the disease.

Within six months of vaccination 21 were found to be tuberculin positive (18 to 3 T.U.), and 19 of these (not shown separately in the table) had a normal radiograph either then or subsequently (two had no radiograph before the disease started). A further five cases were tuberculin positive (four to 3 T.U.) when first tested more than six months after vaccination, and all five had a normal chest radiograph at the same time or subsequently. Of these 26 cases, 20 were found to have in addition a healed vaccination reaction, in two the vaccination site was not examined, and in four (all vole-bacillus-vaccinated) the vaccination reaction was looked for but not found (four, six, six, and 12 months after vaccination respectively).

In 12 cases there were no tuberculin tests after entry and before the disease developed, and therefore no information on whether vaccination produced tuberculin conversion, but 10 had a healed vaccination reaction. In one of the remaining two cases it has not been possible to examine the B.C.G.-vaccination site, and, in the other, the vole-bacillus-vaccination site was examined only 24 months after entry to the trial, when no reaction was observed; a reaction may nevertheless have occurred and subsequently disappeared (M.R.C., 1956).

In summary, these last two cases of the 38 may not have been satisfactorily vaccinated, as judged by the usual criteria. It should be added that one B.C.G.-vaccinated case had a starting-point three months after vaccination; for this, the only case in a vaccinated participant within 12 months of vaccination, the disease could well have arisen before any protection had been conferred.

The Forms of Tuberculosis

The forms of tuberculosis which occurred in the various trial groups are shown in Table IV. If two or more were present, the case was assigned to the major form—for example, tuberculous meningitis took precedence over any other form, and pulmonary tuberculosis took precedence over a pleural effusion.

Seventy per cent. of the cases (245 of 349) were of pulmonary tuberculosis. There is no evidence of any important differences between the five trial groups in this percentage.

Tuberculous pleural effusion, without pulmonary tuberculosis, was the next most numerous form, with 59 cases (17%). In addition, a pleural effusion preceded, or was discovered at the same time as, the pulmonary lesions in 13 more cases (not identified separately in the table). The ratio of pleural effusions to total cases was greatest in the negative unvaccinated group (44 of 153, or 29%) and least among those initially positive to 3 T.U. (12 of 128, or 9%), this difference being significant at the 0.1% level. There were eight pleural effusions among the 38 cases in the vaccinated groups combined, and eight among the 30 cases initially positive only to 100 T.U. There was no significant difference in the ratio of pleural effusions to total cases between the vaccinated and the negative unvaccinated groups.

There were two cases of hilar gland enlargement, with no other lesion, both in the negative unvaccinated group. Hilar gland enlargement was also found, however, in association with other lesions (mainly pulmonary lesions, pleural effusions, or both) in 34 more cases (not identified separately in the table). In all, hilar gland enlargement was noted most frequently among the cases in the negative unvaccinated group (27 of 153, or 18%) and least frequently among those initially positive to 3 T.U. (two of 128, or 2%), this difference being significant at the 0.1% level. Hilar gland enlargement was noted in three of the 38 cases in the vaccinated groups combined and in four of the 30 cases initially positive only to 100 T.U. There was no significant difference in the ratio of hilar gland enlargements to total cases between the vaccinated and the negative unvaccinated groups.

Twelve cases of tuberculous cervical adenitis (one associated with tuberculous tonsils) occurred in the group initially positive to 3 T.U., and three in the negative unvaccinated group; none occurred in any of the other groups.

There were five cases of tuberculous meningitis—four in the negative unvaccinated group and one (41 months after entry) in the group initially positive to 3 T.U. In addition, five of the pulmonary lesions were of miliary type; four of these were in the negative unvaccinated group and one (with a starting-point 57 months after entry) in the group initially positive to 3 T.U. Thus, tuberculous meningitis or miliary tuberculosis occurred in eight of the 153 cases in the negative unvaccinated group and in two of the 128 cases in the group initially positive to 3 T.U. None occurred in the vaccinated groups, or in the group initially positive to 100 T.U.

Nature, Initial and Maximal Extent of the Pulmonary Lesions

The assessor classified the pulmonary lesions according to both their initial and their maximal extent. The *initial* extent was that seen on the first abnormal chest radiograph, a substantial proportion of these being 35-mm. radiographs. If a full-size chest radiograph had been taken within six weeks after the abnormal 35-mm. radiograph, the assessments of cavitation and extent were made instead from the full-size radiograph, because of the difficulty of making an accurate classification from a miniature film. (In a few instances a "5- by 4-in." (12.5- by 10-cm.) film was used similarly for the assessments, if no suitable full-size radiograph was available.) In all, 54 (22%) of the assessments of initial extent were made only from a 35-mm. radiograph; these included 12 cases which subsequently developed cavitation, no cavitation having been seen on the abnormal 35-mm. radiograph.

The nature and *initial* radiographic extent of the pulmonary lesions are shown in Table V. Of the total of 245 pulmonary cases, 5, just referred to, were of miliary type, and 51 (21%) showed cavitation on the first abnormal radiograph. Lesions with cavitation were observed in 25% of the 100 cases in the negative unvaccinated group; in 22% of the 27 cases in the vaccinated groups combined; and in 17% of the 117 cases in the groups initially positive to 3 T.U. or 100 T.U. There is thus no evidence of important differences in the presence of cavitation between cases in the different groups.

Lesions involving more than two rib interspaces (with or without cavitation, and including the miliary cases) were observed on the first abnormal film in 26 (26%) of the 100 cases in the negative unvaccinated group, compared with 3 (11%) of the 27 cases in the vaccinated groups combined; at the other extreme, lesions up to 6 sq. cm. in extent (on a full-size chest radiograph) were observed in 32 (32%) of the cases in the negative unvaccinated group, compared with 13 (48%) of those in the vaccinated groups combined. There is thus a suggestion (which does not attain statistical significance) that in the vaccinated cases the lesions, when first detected, were on average not as extensive as those in the negative unvaccinated group.

The nature and the *maximal* radiographic extent of the pulmonary lesions are shown in Table VI. Comparison with Table V shows that cases with cavitation (on one or more postero-anterior radiographs) had increased from 51 to 79 since the first abnormal radiograph. (Tomograms were not taken as a routine; to avoid bias in comparing the severity of

TABLE IV.—*Definite Cases of Tuberculosis Starting Within Five Years of Entry to the Trial, According to Form of Disease*

Trial Group	Form of Tuberculosis										
	Total Cases	Pulmonary Tuberculosis		Tuberculous Pleural Effusion*	Hilar Gland Enlargement†	Tuberculous Meningitis	Bone or Joint Tuberculosis	Tuberculous Cervical Adenitis	Tuberculous Peritonitis	Erythema Nodosum	Other Forms
		No.	%								
Negative unvaccinated	153	100	65	36§	2	4	2‡	3	2‖	3	1¶
Negative, B.C.G. vaccinated	27	20	74	5	0	0	0	0	1	1	0
Negative, vole bacillus vaccinated	11	7	64	3	0	0	1	0	0	0	0
Positive to 3 T.U.	128	97	76	9	0	1	3	11	1	0	6**
Positive only to 100 T.U.	30	21	70	6	0	0	2	0	0	0	1††
All groups	349	245	70	59	2	5	8	14	4	4	8

* Without evidence of pulmonary tuberculosis. † Without other evidence of tuberculosis. ‡ One with erythema nodosum. § Three with erythema nodosum. ‖ One with small associated pulmonary lesion. ¶ Tuberculous bronchiectasis. ** one tuberculous endobronchitis; one tuberculous tonsils and cervical glands; one lupus vulgaris; three genito-urinary tuberculosis. †† Tuberculous axillary adenitis.

TABLE V.—*Definite Cases of Pulmonary Tuberculosis Starting Within Five Years of Entry to the Trial, According to the Nature and Extent of the Pulmonary Lesions Seen on the First Abnormal Chest Radiograph*

Trial Group	Total Pulmonary Cases	Miliary Type of Lesions	Lesions with Cavitation			Lesions without Cavitation		
			Lesions Involving More than 2 Rib Interspaces	Lesions More than 6 sq. cm. in Extent Involving Up to 2 Rib Interspaces	Lesions Up to 6 sq. cm. in Extent	Involving More than 2 Rib Interspaces	More than 6 sq. cm. in Extent, Involving Up to 2 Rib Interspaces	Up to 6 sq. cm. in Extent
Negative unvaccinated	100	4	18	6	1	4	36	31
Negative, B.C.G. vaccinated	20	0	2	2	1	0	6	9
Negative, vole bacillus vaccinated	7	0	1	0	0	0	3	3
Positive to 3 T.U.	96*	1	8	7	1	8	37	34
Positive only to 100 T.U.	21	0	1	3	0	1	11	5
All groups	244*	5	30	18	3	13	93	82

* Excluding one patient for whom the extent of the lesions was not classified because the first abnormal radiograph, taken before a thoracoplasty was performed, could not be found; the diagnosis was confirmed bacteriologically.

TABLE VI.—*Definite Cases of Pulmonary Tuberculosis Starting Within Five Years of Entry to the Trial, According to the Nature and Maximal Extent of the Pulmonary Lesions*

Trial Group	Total Pulmonary Cases	Miliary Type of Lesions	Lesions with Cavitation			Lesions without Cavitation		
			Lesions Involving More than 2 Rib Interspaces	Lesions More than 6 sq. cm. in Extent Involving Up to 2 Rib Interspaces	Lesions Up to 6 sq. cm. in Extent	Involving More than 2 Rib Interspaces	More than 6 sq. cm. in Extent, Involving Up to 2 Rib Interspaces	Up to 6 sq. cm. in Extent
Negative unvaccinated	100	4	22	10	1	10	31	22
Negative, B.C.G. vaccinated	20	0	5	0	1	0	6	8
Negative, vole bacillus vaccinated	7	0	1	2	0	0	2	2
Positive to 3 T.U.	96*	1	19	12	0	4	44	16
Positive only to 100 T.U.	21	0	1	5	0	2	8	5
All groups	244*	5	48	29	2	16	91	53

* See footnote to Table V.

the lesions in the different groups, evidence of cavitation obtained only from tomograms has therefore been disregarded.) Many of the lesions had also increased in extent since the first abnormal radiograph; lesions which involved more than two rib interspaces (with or without cavitation) had increased from 43 to 64, and lesions with an extent of 6 sq. cm. or less had decreased from 85 to 55.

Lesions with cavitation were now observed in 33% of the 100 cases in the negative unvaccinated group, in 33% of the 27 cases in the vaccinated groups combined, and in 32% of the 117 cases in the tuberculin-positive groups combined. There is again no evidence of important differences in the presence of cavitation between cases in the different groups.

On the other hand, lesions involving more than two rib interspaces (with or without cavitation, and including the miliary cases) were now observed in 36 (36%) of the cases in the negative unvaccinated group, in six (22%) of the cases in the vaccinated groups combined, and in 27 (23%) of the cases in the tuberculin-positive groups combined; at the other extreme, lesions up to 6 sq. cm. in extent were observed in 23 (23%) of the cases in the negative unvaccinated group, in 11 (41%) of those in the vaccinated groups, and in 21 (18%) of those in the tuberculin-positive groups. There is again a suggestion (which does not attain statistical significance) that pulmonary tuberculosis was on average rather less extensive in the vaccinated than in the unvaccinated cases. In other words, the degree of protection from vaccination for the extensive lesions was at least as great as, and may have been greater than, that for the less extensive lesions.

Action Taken by the National Health Service Physician Assuming Charge of the Patient

Further evidence of the serious nature of many of the cases of tuberculosis which occurred is provided by Table VII. Of the 349 patients, 243 (70%) were taken off work for at least three months by the physician assuming charge of the patient. Of these 243 patients, 222 received chemotherapy, collapse therapy, or surgical treatment, in addition to rest in bed; 14 of the remaining 21 were cases of pleural effusion. At the other extreme, 84 patients (24%) remained at work and were kept under observation; 18 of these patients also received some chemotherapy.

Of the 153 patients in the negative unvaccinated group, 73% were taken off work for three months or more, compared with 58% of the 38 patients in the vaccinated groups combined, and 69% of the 158 in the tuberculin-positive groups combined. There is thus again a suggestion (not statistically significant) that the cases were less severe in the vaccinated than in the unvaccinated. In other words, the degree of protection from vaccination for the severe lesions was at least as great as, and may have been greater than, that for the less severe lesions.

TABLE VII.—*Definite Cases of Tuberculosis Starting Within Five Years of Entry to the Trial, According to the Action Taken by the Clinician*

Trial Group	Total Cases	Taken Off Work		Remaining at Work Under Observation
		For 3 Months or More	For Less Than 3 Months	
Negative unvaccinated	153	112	7	34*
Negative, B.C.G. vaccinated	27	15	1	11*
Negative vole bacillus vaccinated	11	7	0	4
Positive to 3 T.U.	128	86	12	30*
Positive only to 100 T.U.	30	23	2	5
All groups	349	243	22	84

* Including one patient who failed to attend the clinic for complete investigation.

Bacteriological and Pathological Investigations

Of the 245 cases of pulmonary tuberculosis, 18 had no bacteriological examination at any time. Positive bacteriological results were obtained in 92 of the remaining 227 cases—in 67 on culture and in 25 only on direct microscopic examination. In 10 of the 135 with negative results the examinations were made only after the start of chemotherapy, but all the other 125 had negative results (76 from culture of laryngeal swab or gastric lavage, 18 on direct examination, and 31 on culture of sputum) at a time when no chemotherapy had been given. Since the investigation and treatment of all cases were carried out at local chest clinics and were not the responsibility of the M.R.C. team physicians, there was no opportunity for the latter to initiate intensive bacteriological examinations, and in many instances no special emphasis was laid upon these tests in the routine management of the cases. As a consequence, the proportion of cases confirmed bacteriologically is low.

In all, tubercle bacilli were isolated from 39 of the 100 cases of pulmonary tuberculosis in the tuberculin-negative unvaccinated group, from nine of the 20 cases in the B.C.G.-vaccinated group, from three of the seven in the vole-bacillus-vaccinated group, from 31 of the 97 in those positive to 3 T.U., and from 10 of the 21 in those positive only to 100 T.U. The organisms isolated

from the nine cases in the B.C.G.-vaccinated group and from the three in the vole-bacillus-vaccinated group were found to be virulent and of human type.

A specimen of the fluid was examined in only 36 of the 59 cases of pleural effusion classified as tuberculous; in 32 the fluid was sterile, and in 23 of these a high proportion of lymphocytes was recorded; in the other four cases (none vaccinated) tubercle bacilli were cultured from the fluid. In six of the eight cases of tuberculosis of bones or joints, and in 10 of the 14 cases of cervical adenitis, the diagnosis was established by histological examination; in one of the remaining four cases of cervical adenitis the diagnosis was confirmed bacteriologically. Of the five cases of tuberculous meningitis, four were confirmed by bacteriological examination of the cerebrospinal fluid, and one at the post-mortem examination (see "Death from Tuberculosis," p. 382).

Reliability of the Independent Assessments

It is conceivable that the withholding of the information on the results of skin tests, essential though it is for an unbiased comparison between the various groups, might have resulted in some cases being incorrectly diagnosed by the assessor. As in the previous report, therefore, his diagnosis is compared with that of the chest clinic or other physician taking charge of the case. For 332 (95%) of the 349 definite cases of tuberculosis arising after entry and accepted for this report, there was agreement on diagnosis between assessor and physician in charge. In addition to the 349 cases, however, a further 13 were regarded by the physician in charge, but not by the assessor, as definite tuberculosis.

Incidence of Tuberculosis in Different Periods Since Entry to the Trial

As already described, the assessor decided retrospectively, from the detailed records of each case of tuberculosis, the date of the earliest radiographic or clinical manifestation of the disease. This has been regarded as the starting-point of the illness. Because the starting-point does not necessarily represent the true (and unknown) date of onset of the disease, the number of cases with starting-points in a given period will depend partly upon the intensity of radiographic examination of participants during that period. Since this intensity has not differed from group to group, the incidence rates in different trial groups *in a particular period of time* may validly be compared. However, the intensity of radiographic examination has shown some decline in the course of the trial, and caution must therefore be exercised when comparing the incidence rates in a particular trial group *from one period to another.*

Table VIII gives the numbers of definite cases of tuberculosis with starting-points in the first and second periods of two and a half years since entry to the trial, with corresponding incidence rates (also illustrated in Figs. 1 and 2). The table and the figures also contain some preliminary information for a third period, from five to seven and a half years after entry. Although the information is incomplete for this period, the annual incidence rates have been calculated by taking into account the varying periods of observation for participants beyond the first five years.

During the first two and a half years the annual incidence in the negative unvaccinated group was 1.98 per 1,000, in the B.C.G.-vaccinated group 0.43 per 1,000, and in the vole-bacillus-vaccinated group 0.42 per 1,000 (Fig. 1). The incidence in the two vaccinated groups combined was 21% of that in the negative unvaccinated group. During the second two and a half years the corresponding rates were 2.62, 0.34, and 0.24 per 1,000; the incidence in the two vaccinated groups combined was 12% of that in the negative unvaccinated group. There is clearly no evidence of any waning in the protection afforded by either of the vaccines up to five years after vaccination. The incomplete figures for the period between five and seven and a half years also show no evidence of any serious decline in protection, the incidence in the two vaccinated groups combined being 24% of that in the negative unvaccinated group.

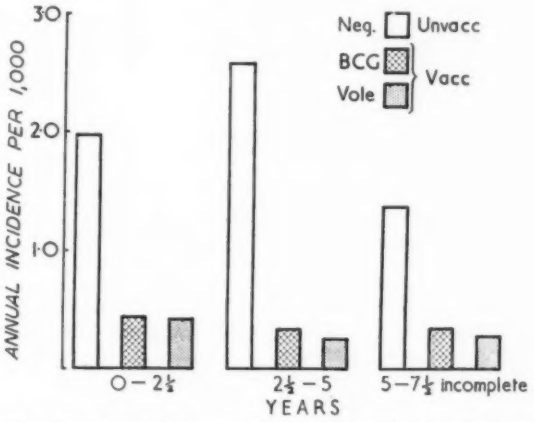

FIG. 1.—Annual incidence of tuberculosis in the negative unvaccinated and the two vaccinated groups.

TABLE VIII.—*Definite Cases of Tuberculosis, According to the Interval Between Entry and the Earliest Radiographic or Clinical Manifestation (the Starting-point) of the Illness*

Trial Group	Estimated No. of Participants	Total Cases: Starting Within 2½ Years of Entry*	Total Cases: Starting Between 2½ and 5 Years After Entry	Total Cases: Starting Between 5 and 7½ Years After Entry (Incomplete)	Annual Incidence per 1,000 Participants: 0–2½ Years	2½–5 Years	5–7½ Years
Negative unvaccinated	13,300	66	87	30	1·98	2·62	1·38
Negative, B.C.G. vaccinated	14,100	15	12	8	0·43	0·34	0·34
Negative, vole bacillus vaccinated	6,700	7	4	3	0·42	0·24	0·29
Positive to 3 T.U. Induration 15 mm. or more in diameter	7,200	63	30	10	3·50	1·67	0·88
Positive to 3 T.U. Induration 5–14 mm. in diameter	8,800	17	18	6	0·77	0·82	0·44
Positive only to 100 T.U.	6,600	12	18	8	0·73	1·09	0·76
All groups	56,700	180	169	65	—	—	—

* These figures are slightly greater than those for the first two and a half years given in the first report (M.R.C., 1956) as a result of more recent information.

The average duration of observation of the participants so far is six and a half years. Protection from both vaccines has therefore remained at a high level for at least this length of time.

Turning to the groups with positive reactions to tuberculin initially, those with the largest reactions (15 mm. induration or more to 3 T.U.) have been separated in Table VIII and Fig. 2 from those with

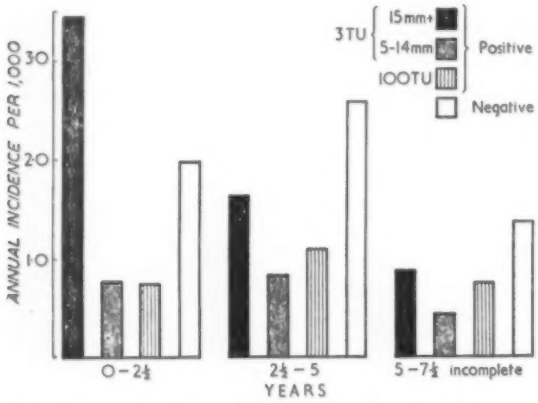

FIG. 2.—Annual incidence of tuberculosis in initially positive and negative unvaccinated groups.

smaller reactions to 3 T.U., because they were found in the first report (M.R.C., 1956) to have a particularly high incidence of tuberculosis in the first two and a half years. During this period the annual incidence in this subgroup was 3.50 per 1,000, substantially greater than that among the negative unvaccinated group (1.98 per 1,000). It was very much greater than the rates among those with smaller reactions to 3 T.U. (0.77 per 1,000), as well as among those positive only to 100 T.U. (0.73 per 1,000). During the second two and a half years the incidence in the group with the larger initial reactions to 3 T.U. (1.67 per 1,000) was now substantially *less* than that in the negative unvaccinated group (2.62 per 1,000); the rate still was greater than the rates of 0.82 and 1.09 per 1,000 among the two groups with weaker positive reactions. On the basis of the incomplete information for the period between five and seven and a half years, the incidence in the group with the larger initial reactions to 3 T.U. was still rather greater than the rates in the two groups with weaker positive reactions; as in the preceding period, it was less than that in the negative unvaccinated group. It will be noted that in each of the three periods the lowest rates were those among the vaccinated participants.

In interpreting the trends in incidence from period to period, a number of points must be considered. First, there is the steep increase in the total incidence of tuberculosis between the ages of 15 and 20 years, and one might therefore expect an increase in at least some of the trial groups. On the other hand, there has been in England a fall in the risk of exposure to tuberculosis in this age group (as indicated by notification data) from about 1952 onwards. Finally, the general slight decline in the intensity of follow-up during the course of the trial (see "Follow-up of Participants," p. 380) may have enhanced any decline, and detracted from any increase, in the incidence rates.

Considering first the group with the larger reactions to 3 T.U. initially, and taking these points into account, these seems no doubt of the steep decline in incidence from the high initial rate. (The different forms of tuberculosis appear to have declined to a similar extent in this group; between the first and second periods of two and a half years, the number of cases of pulmonary tuberculosis decreased from 47 to 23, the cases of pleural effusion from three to two, and the other cases from 13 to five.) In contrast, the rates in the two groups with weaker positive reactions initially have remained at much the same level during the whole period of seven and a half years, with the result that the rates in all three initially tuberculin-positive groups are now not markedly different.

In the negative unvaccinated group, an increase betwen the first and second periods of two and a half years, and a larger decrease between the second and the third period, have been apparent. Parallel with this there has been little change in the rates in the two vaccinated groups. It is difficult to decide the relative contributions of the factors referred to above in explaining these trends.

III. MORTALITY AND MORBIDITY FROM CAUSES OTHER THAN TUBERCULOSIS

Deaths from Causes Other than Tuberculosis

The number of participants known to have died within five years of entry to the trial is 126: one from tuberculosis (see p. 382), 70 from other diseases, and 55 from accidental causes or on active military service. Of the 70 deaths from non-tuberculous diseases, 22 were due to malignant disease; no other individually classified cause was responsible for as many as 10 deaths.

Table IX shows that the mortality from non-tuberculous diseases was less in each of the vaccinated groups than in the corresponding negative unvaccinated group, but the numbers are small and the differences are not statistically significant. The mortality among those who were tuberculin positive (to either 3 or 100 T.U.) was rather greater than among those who were tuberculin negative on entry (whether vaccinated or not); for Section A of the table the difference is significant at the 5% level.

Table IX also shows that the mortality from accidental causes (including deaths on active military service) was similar in each of the vaccinated groups and in the corresponding unvaccinated group. There was no great difference in the mortality between those who were tuberculin positive (to either 3 or 100 T.U.) and those who were tuberculin negative on entry (whether vaccinated or not).

Cases of Non-tuberculous Diseases

A total of 152 cases, when submitted to the assessor, were classified by him as not due to tuberculosis. These consisted mainly of chest diseases such as pneumonia, bronchiectasis, and pleurisy, submitted because the radiographic abnormality persisted for more than 14 days (see "Records of Cases," p. 381), but they included also a few non-pulmonary lesions where tuberculosis, although a possible diagnosis, was not accepted by the assessor.

Table IX shows that there are no more than chance differences between the rates in the various trial groups, and indicates that there is no protective effect of B.C.G.

or vole bacillus vaccine against these non-tuberculous diseases, when taken as a group. The principal categories were pneumonitis and other non-specified pulmonary lesions (62 cases), pneumothorax (22 cases), non-tuberculous pleural effusions (as judged by duration, resolution with non-tuberculous chemotherapy, etc.—18 cases), bronchiectasis and allied lesions (16 cases), and definite or possible sarcoidosis (seven cases). Analysis of the figures for each of these categories separately suggests that vaccination does not influence the incidence of disease in any of them. For example, three of the pleural effusions were in the negative unvaccinated group and five in the two vaccinated groups combined; nine occurred among those initially positive to 3 T.U., and one among those positive only to 100 T.U.

The final column of Table IX shows the distribution of the 34 cases, submitted to the assessor as suspected or possible cases of tuberculosis, for which he decided that there was no evidence of any disease, tuberculous or non-tuberculous; the number in each trial group is roughly proportionate to the number of participants in that group.

IV. CRITICAL APPRAISAL OF THE DESIGN OF THE TRIAL

The present investigation was designed to give reliable estimates of the degree of protection afforded by B.C.G. and vole bacillus vaccination, and embodied three main safeguards against bias. These were, first, the random allocation of the tuberculin-negative participants to the unvaccinated and vaccinated groups on entry to the trial; second, the comprehensive scheme for the follow-up of the participants and the detection of cases of tuberculosis and other chest diseases among them, these methods being designed to be equally intensive and comprehensive in all the trial groups; and, third, the system for the independent assessment of all the cases discovered, without any knowledge of skin-test results or of vaccination. It is desirable to examine critically the possibility of any deficiencies in the practical working-out of these safeguards before reliance is placed on the degree of protection revealed.

Before doing so, a general point concerning the background of the investigation will be considered. The trial took place among volunteers, initially not in known contact with tuberculosis at home, approximately 60% of those approached agreeing to participate. It is possible that the effect of vaccination in this selected community may differ from its effect in the whole adolescent and young adult population of Britain. This point cannot be tested directly; but there is indirect evidence that the trial population is not grossly unrepresentative—namely, that when allowance is made for the effects of vaccination, the total of 349 cases of tuberculosis within five years of entry to the trial is of the order of magnitude that would have been expected from the national notification figures (Sutherland, 1959).

Allocation to the Tuberculin-Negative Unvaccinated and Vaccinated Groups on Entry to the Trial

The reason for allocating the tuberculin-negative participants to the unvaccinated or to one of the vaccinated groups, according to the final digit of the serial number on the record card, was to ensure that the allocations were not determined either by any of the team members personally or by the participants themselves, but by an independent process. Care was taken to exclude from the analysis all of the few participants who were allocated to the incorrect group, in case any personal choice might have entered into these allocations. This effectively random allocation process should therefore have resulted in the concurrent admission of similar groups of participants to the negative unvaccinated and the two vaccinated groups, with no more than chance differences between them. Direct checks made on representative samples of the records show that the unvaccinated and vaccinated groups were closely similar on entry in their distributions by age, sex, and number of brothers and sisters.

Intensity of Follow-up and Case-finding Procedures

It was shown in the first report (M.R.C., 1956, Table II) that the success of the follow-up during the first 18 to 24 months after entry was similar in those concurrently admitted to the negative unvaccinated and the two vaccinated groups. Recent analysis of a further random sample of the records has also shown no appreciable differences between the negative unvaccinated and the two vaccinated groups in the proportions of the participants brought in contact with the teams, or given chest radiographs, in the period 1957–8. It may be concluded that the co-operation of the participants has been similar in these groups throughout the trial; there is thus no reason to believe

TABLE IX.—*Deaths from Causes Other than Tuberculosis and Cases Assessed as Diseases Other than Tuberculosis Within Five Years of Entry to the Trial; also Cases Assessed as Having No Evidence of Any Disease*

Section *	Trial Group	Estimated No. of Participants	Deaths from Diseases Other Than Tuberculosis†		Deaths From Accidental Causes		Cases Assessed as Diseases Other Than Tuberculosis		Cases Assessed as No Disease
			No. Occurring Within 5 Years	Annual Mortality per 1,000 Participants	No. Occurring Within 5 Years	Annual Mortality per 1,000 Participants	No. Starting Within 5 Years	Annual Incidence per 1,000 Participants	
A Children admitted concurrently with those given B.C.G. vaccine	Negative unvaccinated	13,200	16	0·24	12	0·18	35	0·53	9
	Negative, B.C.G. vaccinated	14,100	8	0·11	16	0·23	42	0·60	7
	Positive to 3 T.U.	15,800	25	0·32	15	0·19	49	0·62	12
	Positive only to 100 T.U.	6,500	12	0·37	10	0·31	17	0·52	3
B Children admitted concurrently with those given vole bacillus vaccine	Negative unvaccinated	6,500	10	0·31	4	0·12	18	0·55	2
	Negative, vole bacillus vaccinated	6,700	7	0·21	3	0·09	9	0·27	3
	Positive to 3 T.U.	8,800	19	0·43	9	0·20	19	0·43	7
	Positive only to 100 T.U.	3,600	5	0·28	4	0·22	7	0·39	1

* Many participants, deaths, cases of diseases other than tuberculosis, and cases with no evidence of disease appear in both sections of this table (see text), and the figures from the two sections can therefore not be totalled.

† There was one death from tuberculosis within five years of entry (see text).

that the numbers of cases reported have been affected by any differences in the intensity of the case-finding procedures from group to group.

Knowledge by the Physician of the Skin-test and Vaccination State

As described in the first report (M.R.C., 1956), leaflets explaining the scheme were distributed to the children before it started. In addition, those vaccinated were given other leaflets describing the normal course of the vaccination reaction, and the vaccination sites were later examined. It is conceivable that this knowledge could have influenced the comparisons between the groups. For example, believing themselves to be protected, those vaccinated might have taken less care to avoid exposure to infection; this would tend to reduce the apparent degree of protection. In the same belief, they might alternatively have been less ready to attend for radiographic examination, or to report any symptoms; this would tend to exaggerate the degree of protection.

The data provide some evidence on the latter possibility. First, as stated above, the amount of co-operation, and in particular the proportions who had routine chest radiographs taken by the M.R.C. teams, were similar in the vaccinated and the unvaccinated groups. Secondly, the first section of Table X shows the total of 191 cases of definite tuberculosis starting within five years of entry in the negative unvaccinated and the two vaccinated groups, subdivided into the cases which were discovered because the participants sought medical attention from the National Health Service for symptoms—that is, where the participants knew they were ill—and into those which were discovered only as a result of a routine chest radiograph (whether taken by the M.R.C. teams or elsewhere)—that is, where the participants were unaware that they were ill. The final line of Table X shows the percentage reduction in the incidence of tuberculosis, attributable to vaccination, for each method of discovery. The degree of protection for participants who were aware of their illness was closely similar to that for participants who were unaware of it; this does not suggest that the vaccinated participants ignored their illnesses.

Further, if there was any suppression of illnesses by vaccinated participants, this would presumably occur mainly with the less extensive and less severe lesions; the degree of protection would thus appear to be greater for these than for the other lesions. It has already been found, on the contrary, that the degree of protection is *not* greater for the less extensive and severe lesions, as judged by their radiographic extent and the action taken by the physician in charge (see "Extent of the Pulmonary Lesions," p. 385, and "Action Taken by the Physician," p. 386).

Knowledge by the Physician of the Skin-test and Vaccination State of the Participant

Physicians in the National Health Service

For those cases which were first discovered by the usual methods of the National Health Service, it is possible that the physician might have been influenced in making the diagnosis by knowledge of the patient's participation in the trial, and of the skin-test and vaccination state. However, the follow-up scheme through the chest clinics ensured that both tuberculous and non-tuberculous diagnoses would have come to the notice of the M.R.C. teams for review of the case by the assessor. The diagnoses of the National Health Service physician can therefore validly be compared with those of the independent assessor. Of the total of 124 National Health Service cases accepted as definite tuberculosis by the assessor, two were regarded by the National Health Service physician as only possibly due, and three as not due, to tuberculosis, and in a further case no diagnosis was made; three of these six disagreements occurred among the 21 cases in the two vaccinated groups combined. On the other hand, three cases (not included in the 124) were regarded by the National Health Service physician as definite tuberculosis; the assessor regarded two of these as possibly due to tuberculosis, and one as inactive tuberculosis, present on entry, with no evidence of subsequent activity; two of these three disagreements occurred in vaccinated participants. Thus any knowledge of skin-test results or of vaccination on the part of the National Health Service physicians has not influenced the results appreciably.

M.R.C. Team Physicians

It has been suggested (Palmer, Shaw, and Comstock, 1958) that knowledge of the skin-test and vaccination state by the M.R.C. team physicians may have led them to select which cases were to be submitted to the independent assessor, and thereby to introduce a bias between the tuberculin-negative unvaccinated and the vaccinated groups.

Knowledge of the skin-test and vaccination state of the participants was indeed readily available to the teams. If this had influenced the diagnoses of the team physicians—and had thereby affected which of their cases were submitted to the assessor—a different

TABLE X.—*Definite Cases of Tuberculosis in the Negative Unvaccinated and the Two Vaccinated Groups within Five Years of Entry, Subdivided* (a) *According to the Method of Discovery of the Disease,* (b) *According to the Physician First Diagnosing the Case, and* (c) *According to the Trial Area*

Trial Group	Total Cases of Definite Tuberculosis	Method of Discovery of Disease		Physician First Diagnosing Case		Area		
		Medical Attention Sought for Symptoms	Routine Chest Radiograph	National Health Service	Medical Research Council	London	Birmingham	Manchester
Negative unvaccinated	153	71	82	103	50	37	67	49
Negative, B.C.G. vaccinated	27	11	16	14	13	7	7	13
Negative, vole bacillus vaccinated	11	4	7	7	4	—	4	7
Total ..	191	86	105	124	67	44	78	69
Percentage reduction in incidence of tuberculosis attributable to vaccination ..	*84*	*86*	*82*	*87*	*78*	*81*	*91*	*78*

degree of protection might be expected for cases first discovered by the team physicians and for those first discovered by the National Health Service. The relevant subdivision of the total cases of definite tuberculosis is made in the second section of Table X. The final line shows a similar degree of protection for the cases discovered in the two ways.

Supplementary evidence on this point is provided by the third section of Table X, in which the cases of definite tuberculosis are subdivided according to the three main areas of the study; the degree of protection afforded by vaccination is of the same high order in all three. The conduct of the trial in each area was the responsibility of a different M.R.C. team physician, and the findings thus do not indicate that there was any differential bias between these physicians.

Finally, as has been emphasized (see "Records of Cases," p. 381), *all* cases with a pulmonary radiographic abnormality persisting for at least 14 days were submitted to the assessor. Moreover, all 35-mm. as well as full-size chest radiographs of the participants have been read separately by a physician unconnected with the trial and unaware of the skin-test or vaccination state of any participant, as well as by the team physician (see "Follow-up of Participants," p. 380. A persistent abnormality found by either reader qualified the case for submission to the assessor. With this comprehensive system, any unconscious suppression of cases of tuberculosis by the team physician is highly improbable.

The Independent Assessor

There remains the possibility that the independent assessment was itself in some way biased. However, the assessor was rigorously kept unaware of the results of any tuberculin tests and of whether any vaccination had been performed. Moreover, as already stated, these "blind" assessments showed a very substantial difference in the incidence of definite tuberculosis between the negative unvaccinated and the vaccinated groups (Table I), but no important differences in the incidence of cases and deaths from non-tuberculous causes (Table IX).

V. ESTIMATED BENEFITS OF VACCINATION

From the foregoing critical appraisal it appears justifiable to conclude that no serious bias has entered into the comparison between the unvaccinated and vaccinated groups, and that their difference in incidence of tuberculosis may be confidently attributed to the vaccination.

On the basis of this conclusion it is permissible to assign limits of chance fluctuation to the observed degree of protection afforded by each of the two vaccines. The percentage reduction in the incidence of tuberculosis in the B.C.G.-vaccinated group, compared with the incidence in those concurrently admitted to the negative unvaccinated group, was 83% for the five-year period following vaccination. Making allowance for chance fluctuations in the numbers of cases observed, it is possible to say with a high degree of confidence (99%) that the protection afforded by B.C.G. vaccination in the tuberculin-negative section of the population studied lay between 71% and 90%.

The corresponding estimate for the degree of protection afforded by vole bacillus vaccination was 87%. Allowing for chance fluctuations, it is very likely (99%) that the protection lay between 73% and 96%.

In any mass-vaccination scheme this protection would apply only to the tuberculin-negative section of the population. There would be no direct effect on the number of cases among those who were already tuberculin positive at the pre-vaccination test (and therefore ineligible for vaccination); in assessing the total contribution of vaccination to the reduction in incidence of tuberculosis these cases must be taken into account. In the present trial 158 cases of tuberculosis were found in such tuberculin-positive participants within five years of entry; this represents 29% of the total of 550 cases expected in the trial population if no vaccination had been given (see next paragraph).

According to the present results, if *none* of the tuberculin-negative entrants had been vaccinated, 392 cases would have been expected among them within five years. If *all* of them had received B.C.G. vaccine, 65 cases would have been expected among them, or, if all had received vole bacillus vaccine, 56 cases. Including the 158 cases observed among the tuberculin-positive entrants within five years of entry with each of these estimates, the reduction in the total number of cases within five years of entry would have been from 550 (392 plus 158) to 223 (65 plus 158) with B.C.G. vaccination, or to 214 (56 plus 158) with vole bacillus vaccination. This represents a reduction of 59% with B.C.G. vaccine, or of 61% with vole bacillus vaccine, in the incidence of tuberculosis in the entire trial population—that is, in the tuberculin-negative and tuberculin-positive groups combined—for the five-year period. The figure of 59% corresponds to that of 55% for B.C.G. vaccine for the first two and a half years, given in the first report (M.R.C., 1956).

The above estimate has been calculated after the exclusion of 150 previously unsuspected cases of definite tuberculosis which were present on entry to the trial, this being discovered in the great majority because there was an initial radiographic examination (70 excluded at the time of entry plus 80 excluded subsequently by the assessor—see "Cases of Tuberculosis Present on Entry," p. 381). If the preliminary radiograph had not been taken, many of these cases would apparently have arisen after entry, and would have increased the total cases among those tuberculin positive from 158 to a figure of the order of 300. The apparent reduction in the incidence of tuberculosis, as a result of vaccinating all those who were initially tuberculin negative, would in these circumstances have been of the order of 50% with each vaccine, instead of the 60% estimated above.

VI. DISCUSSION

In this second report of the Medical Research Council's Tuberculosis Vaccines Clinical Trials Committee, the period of observation of the participants is extended from two and a half years (M.R.C., 1956) to five years after entry to the trial. The results show that the two vaccines conferred substantial protection against tuberculosis for this period in a large group of adolescents living under the ordinary urban and suburban conditions prevailing in industrial communities in Britain; the reduction in incidence in the vaccinated group, compared with the tuberculin-negative unvaccinated group, was 83% for B.C.G. vaccine and 87% for vole bacillus vaccine. Preliminary

incomplete information beyond five years has shown that the protective efficacy of the vaccines has been maintained at a similar high level for at least six and a half years.

Most of the 349 definite cases of tuberculosis known to have started within five years of entry were clinically important, as judged by the form of the disease, its extent, and the treatment given; and the pulmonary lesions in the negative unvaccinated group were clinically as important as those in the initially tuberculin-positive groups. Moreover, the degree of protection from vaccination for the clinically important lesions was certainly as great as (and may even have been greater than) that for the less important lesions. These findings should be set against the doubts expressed by Myers (1957) and again by Anderson *et al.* (1959) that in this trial the protection might apply only to "primary pulmonary infiltrates" and not to clinical tuberculosis.

Seven cases (three of erythema nodosum closely following B.C.G. vaccination, and four of regional adenitis following vole bacillus vaccination) were regarded as complications of vaccination and were not included in the total of 349 cases. It is possible that some or all of these may nevertheless have resulted from infection with virulent tubercle bacilli. If, as an extreme, all seven cases had been regarded instead as cases of tuberculosis in vaccinated participants, the apparent protection against tuberculosis within five years of entry would only have been reduced from 83% to 82% for B.C.G. vaccine and from 87% to 81% for vole bacillus vaccine.

The incidence of non-tuberculous deaths and diseases in the different trial groups has been compared in this report as for tuberculosis. Taken as a whole, such deaths and diseases were found to have a similar incidence in the vaccinated and the tuberculin-negative unvaccinated groups; the mortality was, however, slightly greater in the two tuberculin-positive groups. When the more frequent diagnoses were considered separately, no evidence of protection by B.C.G. or vole bacillus vaccination was revealed against any specific cause of death, nor against any chest disease other than tuberculosis.

The batches of B.C.G. vaccine maintained a satisfactory protective potency, despite routine fluctuations in viable count and corresponding slight variations in the degree of post-vaccination tuberculin sensitivity. The data provide no information on the level of viable count at which protective efficacy would show a decline. It is of particular interest that the early batches of vole bacillus vaccine, which were unintentionally weaker than the later batches, also conferred a high degree of protection against tuberculosis. Thus these "sub-standard" batches, or possibly even weaker batches still, could have been used throughout the trial, and would have provided substantial protection, despite the low level of tuberculin sensitivity which they produced. This finding has important practical implications for the assessment of vole bacillus vaccine. The routine use of this vaccine seemed to be contraindicated (M.R.C., 1956) because of the occurrence of lupus vulgaris at the site of vaccination in a number of cases. Such complications, however, occurred only among the participants receiving the later, stronger vaccine, none being observed among those receiving the earlier, weaker vaccine. This weaker vole bacillus vaccine has therefore proved both safe and effective, in agreement with the experience of Sula (1958), using an attenuated strain of the vole bacillus.

From the data just discussed it also appears that the protective efficacy of vole bacillus vaccine cannot necessarily be gauged by the degree of post-vaccination tuberculin sensitivity, at least to human tuberculin. The same conclusion is not justified for B.C.G. vaccine, since even the weakest batches produced an acceptably high degree of post-vaccination sensitivity (76% to 3 T.U. and 100% to 100 T.U.); a high conversion rate should therefore remain the aim of any B.C.G. vaccination scheme.

Although the vaccinated and the tuberculin-negative unvaccinated groups were alike, except for the fact of vaccination, the groups tuberculin positive on entry differed not only by virtue of their sensitivity but also by the (unknown) previous circumstances which produced that sensitivity. A notable feature of the first report was the high incidence of tuberculosis occurring during the first two and a half years among those participants who entered the trial with high degrees of tuberculin sensitivity (induration of 15 mm. or more to 3 T.U.), which was much greater than among those with weaker positive reactions (5–14 mm. induration to 3 T.U., or positive reactions only to 100 T.U.). A similar contrast was previously noted among African mining recruits (Report of the Tuberculosis Research Committee, 1932), and among young nurses in England (Daniels, Ridehalgh, and Springett, 1948), and has since been reported for other population groups (Frimodt-Moller, 1957; Palmer, 1957; Palmer, Jablon, and Edwards, 1957; Groth-Petersen, 1959). It has now been found that this high incidence of tuberculosis among the highly tuberculin-sensitive entrants has after a few years become markedly reduced, although it is still rather higher than the rates in the groups with lesser sensitivity. This suggests that in any programme for the periodic radiography of adolescents found to be highly sensitive to tuberculin in connexion with the national vaccination scheme for 13-year-old schoolchildren, the highest yield of cases of tuberculosis is likely to be in the first few years of observation.

The initial high incidence of tuberculosis among the participants with high tuberculin sensitivity may well reflect active infections acquired before entry, but not visible on the initial radiograph, a proportion of these giving radiographic manifestations of disease soon after entry. It seems unlikely that many of the active cases in these participants have arisen from a fresh infection sustained after entry, since there is evidence from other studies that the tuberculosis incidence in groups with high levels of initial tuberculin positivity is largely independent of subsequent exposure to tuberculosis. Thus, a substantial incidence has been found in environments where the rate among initially tuberculin-negative persons observed in parallel was relatively low (Frimodt-Moller, 1957; Palmer, 1957; Palmer *et al.*, 1957), as well as in environments where it was relatively high (Daniels *et al.*, 1948). It should be noted that the decline in incidence in the highly tuberculin-sensitive group in the present trial was associated not only with a lengthening interval from the time of the original infection but also with an increase in age from 15–17 years to 20–22 years, and so perhaps with a change in susceptibility.

The comparatively stable low incidence of tuberculosis among those with initial low-grade sensitivity (weak positive reactions to 3 T.U. or positive reactions only

to 100 T.U.) may reflect, in the main, old or subsiding infections, or more recent infections of a minor character. However, whether these or some other explanations apply, it should be noted that these tuberculosis rates were considerably lower throughout the whole period of observation than those in the tuberculin-negative unvaccinated group. This finding suggests that low-grade sensitivity is associated with a naturally acquired specific immunity against fresh exogenous tuberculous infections, of a degree not possessed by those who were tuberculin negative on entry.

It has been suggested (World Health Organization Tuberculosis Research Office, 1955; Palmer, 1957; Edwards and Palmer, 1958) that low-grade tuberculin sensitivity in man is mainly due to previous infection with organisms other than mammalian tubercle bacilli, but closely related antigenically. Latterly it has been further suggested that these "non-specific" infections may confer some degree of antituberculous immunity (Palmer, 1957). This is not the place to enter deeply into this matter, but it should be stated that none of the conclusions from the present trial is inconsistent *either* with the hypothesis that all grades of tuberculin sensitivity concerned are caused by the tubercle bacillus, *or* with the extreme hypothesis that positive reactions of 15 mm. and more to 3 T.U. are tuberculous in origin, while positive reactions of 5–14 mm. to 3 T.U., as well as positive reactions to 100 T.U. but not to 3 T.U., are caused by other organisms (provided that these organisms also confer protection against tuberculosis).

The benefit to be expected from mass-vaccination of a given population—that is, the reduction in the total incidence of tuberculosis—will depend in general upon four main factors, which may vary with circumstances: (1) the basic degree of protection afforded by vaccination to those who are tuberculin negative; (2) the risks run by the latter (if not vaccinated) of acquiring natural tuberculous infection and disease during the ensuing years; (3) the incidence of disease during the ensuing years in those already tuberculin positive at the age at which vaccination is offered; and (4) the relative proportions of individuals tuberculin positive and negative at this age. These factors are to some extent interrelated.

In the present trial, the benefit that would have accrued to the entire population, tuberculin positive and negative combined, during the first five years, had *all* the tuberculin-negative entrants been vaccinated, was estimated as 59% for B.C.G. vaccine and 61% for vole bacillus vaccine. This assessment relates to a large section of the urban population of Britain, whose observation began in 1950–2. Since then there has been a decrease in the exposure to tuberculous infection in the young adult age group, which, by decreasing the cases to be expected in the tuberculin-negative group, and leaving those in the positive groups largely unaffected, would tend to decrease the benefit. But there has also been a notable decline in the prevalence of tuberculin sensitivity to 3 T.U. in those aged 13–15 years (compare M.R.C., 1958, with M.R.C., 1956), which, by increasing the proportion of the population group eligible for vaccination, would tend to increase the benefit. Because of these opposing tendencies, the percentage reduction in total incidence of tuberculosis, as a result of vaccination of a similar group of school-children at the present time, is unlikely to differ substantially from the above figure of about 60% (Sutherland, 1959). As a corollary, however, vaccination at a rather earlier age than 14 years, at which age a smaller proportion would have been infected naturally, would tend to increase the benefit of vaccination.

Since the publication of our first report, other controlled trials of B.C.G. vaccination have progressed further. That in North American Indians by the late J. D. Aronson and his wife concerned about 1,500 tuberculin-negative subjects from infancy to 20 years old who were given B.C.G. vaccine; a similar number were left unvaccinated. The tuberculosis morbidity, judged by annual radiography, was studied for 11 years and the mortality for 20 years (Aronson, Aronson, and Taylor, 1958). The protection against pulmonary tuberculosis was 75% and against death from tuberculosis 82%; since very few deaths had occurred in the latter part of the 20-year observation period, it was difficult to be sure that the protection was maintained beyond the first 10 years. The incidence of non-tuberculous pulmonary lesions was somewhat greater in the control group than among the vaccinated; the non-tuberculous death rate was similar in the two groups.

The follow-up of Muslim children in Algiers, after oral vaccination of half of them at birth and again at the ages of 1 and 3 years, has continued to show an advantage to the vaccinated in mortality from all causes up to the age of 7 years (Sergent, Catanei, and Ducros-Rougebief, 1956). Rosenthal (1955, 1956) has followed 5,737 vaccinated and 4,378 unvaccinated newborn infants in Chicago (of whom 311 and 250 respectively were born into tuberculous households) for periods of up to 18 years; he found a 77% reduction in morbidity and an 81% reduction in mortality in the vaccinated as compared with the control group. To these planned trials, all with results of a similar order to those in the Medical Research Council trial, must be added the unique study by Hyge (1947) of an epidemic in a school which had been partly subjected to prior B.C.G. vaccination; the follow-up has now been extended to 12 years (Hyge, 1956) and is of particular interest in providing some evidence of protection against "post-primary" tuberculosis appearing after a considerable interval.

The preliminary stages of two large trials under the U.S. Public Health Service—in Puerto Rico and in Georgia and Alabama—were mentioned in the first report (M.R.C., 1956). A progress report, summarizing the results during a follow-up period of six to seven years, has now been published (Palmer, Shaw, and Comstock, 1958). In Puerto Rico nearly 200,000 volunteers aged 1–18 years were included; in Georgia and Alabama the 64,000 volunteers were aged 5 and upwards. The results differ from those of the present trial in two principal respects over a similar observation period. First, the proportion of the total cases which arose among the initially tuberculin-positive participants was much greater in the American trials; second, B.C.G. vaccination was found to have a much lower protective efficacy—namely, 31% in Puerto Rico and 36% in Georgia and Alabama, compared with 83% in Britain.

There are many obvious differences between the U.S. Public Health Service trials and the British trial, in the populations studied, the criteria for vaccination, the vaccines used, and the methods of follow-up. Because of these numerous differences in approach, it is difficult to discuss profitably the reasons for the differences in the results until further information

on all three trials has been published. In this connexion, however, an important epidemiological point deserves mention. This is the inclusion, both in the vaccinated and in the control groups in the American trials, of some persons who, while negative to the tuberculin tests used as criteria for vaccination, still had some low-grade tuberculin sensitivity (to 100 T.U.), and possibly a certain degree of specific antituberculous immunity. According to Palmer (1957) the prevalence of such low-grade sensitivity is much greater in the areas covered by the two American trials than in the British investigation. If this factor has contributed to the differing results it follows that in the areas of the U.S.A. where, like Northern Europe, low-grade sensitivity is relatively uncommon (World Health Organization Tuberculosis Research Office, 1955), a similar efficacy to that found in the British trial might have been discovered, had the American investigations taken place there instead of in the southern States and in Puerto Rico.

The main objective of the present trial is to define the extent and duration of the protective efficacy of B.C.G. and vole bacillus vaccination among those who were tuberculin negative on entry. The official national mass-vaccination scheme (Ministry of Health, 1953) for tuberculin-negative schoolchildren aged 13, which in 1958 was responsible for the B.C.G. vaccination of 241,434 children in England and Wales (Ministry of Health, 1959) out of a total of 658,000 of this age, is designed to cover the susceptible years of adolescence; and the duration of protection is thus crucial if revaccination is to be avoided. Duration of protection is also important in relation to the suggestion (Barns, 1955; Griffiths and Gaisford, 1956; Pollock, 1957) that the age for vaccination should be earlier in childhood, in order to anticipate some of the naturally acquired infections already present at age 13. It is therefore our intention to continue this trial in its present form until 1960, in order to provide information on the duration of protection up to eight to 10 years after vaccination.

Tuberculosis is still a major problem in young adults in England and Wales. In 1958, 2,501 new cases were notified among those aged 15–19 years, and 3,414 at ages 20–24 years. These figures underline the scope which still exists for the vaccination of adolescents in Britain.

VII. SUMMARY

A controlled clinical trial of B.C.G. and vole bacillus vaccines in the prevention of tuberculosis in England started in 1950 and is still in progress. The 56,700 participants were initially free both from active tuberculosis and from known contact with the disease at home. On entry they were children, all aged 14 to 15½ years, and about to leave school; they are now (1959) young men and women aged between 21 and 23 years. The great majority have continued to live in their original urban areas, in or near North London, Birmingham, and Manchester, apart from the two-year period of military service, which has involved about two-thirds of the young men. This second report presents results after each participant had been in the trial for five years, with preliminary incomplete information up to seven and a half years.

As a result of an initial examination at school by M.R.C. teams, the participants were automatically classified into five trial groups: tuberculin negative (to 100 tuberculin units—T.U.) and left unvaccinated (13,300 participants); tuberculin negative, B.C.G. vaccinated (14,100); tuberculin negative, vole bacillus vaccinated (6,700); tuberculin positive to 3 T.U. (16,000); and tuberculin positive to 100 T.U. but not to 3 T.U. (6,600). Those tuberculin negative, and thus eligible for vaccination, were allocated to the unvaccinated or to one of the two vaccinated groups by a random process.

The participants in all five trial groups have been followed intensively by means of routine periodic radiographic examinations and tuberculin tests by the M.R.C. teams, individual contact also being maintained by postal inquiries and visits to the home. Cases of tuberculosis and other chest diseases have also been discovered by chest clinic and other National Health Service physicians and by the medical services of the Armed Forces, and have been brought to the notice of the teams by routine inquiries.

All definite and suspected cases of tuberculosis, and all cases of pulmonary radiographic abnormality persisting for more than 14 days, were submitted to an independent assessor for a final diagnosis; to avoid bias, he was kept unaware of the results of all tuberculin tests, and of whether any vaccination had been performed. As an integral part of the present report, a detailed appraisal was made of these and other essential safeguards against bias incorporated into the trial; this showed that no serious bias had entered into the comparisons between the unvaccinated and vaccinated groups, and that their difference in incidence of tuberculosis could be confidently attributed to the vaccination.

A total of 349 definite cases of tuberculosis started within five years of entry to the trial; of these, 70% were of pulmonary tuberculosis and 17% of tuberculous pleural effusion without evidence of pulmonary tuberculosis; 70% of the total cases (73% in the negative unvaccinated group) were severe enough to be taken off work for at least three months; 32% of the pulmonary cases (33% in the negative unvaccinated group) showed cavitation radiographically, and 28% (36% in the negative unvaccinated group) involved more than two rib interspaces. There was one death from tuberculosis in the five-year period.

During the five-year period the annual incidence of tuberculosis in the B.C.G.-vaccinated group was 0.38 per 1,000, compared with 2.29 per 1,000 among those in the tuberculin-negative unvaccinated group who were admitted concurrently; this represents a reduction, attributable to vaccination, of 83%. Over the same period, the annual incidence of tuberculosis in the vole-bacillus-vaccinated group was 0.33 per 1,000, compared with 2.62 per 1,000 among those admitted concurrently to the tuberculin-negative unvaccinated group; this represents a protection of 87%. (The difference in incidence between the two vaccinated groups, when based also on concurrent admissions, could well have arisen by chance.) The protective efficacy of each vaccine was thus substantial and was closely similar to that found for the first two and a half years in the earlier report (M.R.C., 1956). Moreover, the incomplete information beyond five years shows that similar high levels of protection have continued up to at least six and a half years after entry.

The degree of protection was similar for pulmonary tuberculosis, for tuberculous pleural effusion, and for hilar gland enlargement (in association with other

lesions). On the other hand, since four cases of tuberculous meningitis and four of miliary tuberculosis were found among the negative unvaccinated participants, but none among those who were vaccinated, the degree of protection may have been greater for these forms. There is now a suggestion also that the lesions in the vaccinated cases were less extensive (both on the first abnormal radiograph and at their maximal extent) and less severe (as judged by the action taken by the clinician) than those in the negative unvaccinated cases. In other words, the degree of protection for the more extensive and severe lesions was certainly as great as, and may even have been greater than, that for the less extensive and severe lesions.

The proportion of participants reacting to 3 T.U. after B.C.G. vaccination varied slightly with the routine fluctuations in the viable count of the batches used, though virtually all participants converted to 100 T.U. Even the batches with the lowest counts gave substantial protection.

The strength of the early batches of vole bacillus vaccine was below the standard intended, and the conversion rates, both to 3 T.U. and to 100 T.U., were considerably less for these batches than for the later batches. The early batches, nevertheless, conferred substantial protection against tuberculosis, and lupus vulgaris at the site of vaccination (noted in the first report) did not occur with these batches.

Among those with strong positive reactions to 3 T.U. on entry (15 mm. induration or more) the annual incidence of tuberculosis was 3.50 per 1,000 in the first two and a half years, 1.67 in the second two and a half years, and 0.88 in the (incomplete) five to seven-and-a-half year period. In contrast, the annual incidences among those with weaker positive reactions to 3 T.U., and among those positive only to 100 T.U., were respectively 0.77 and 0.73 per 1,000 in the first two and a half years, and remained at much the same level thereafter. Thus, in this age group, those highly sensitive to tuberculin had a special risk of developing tuberculosis during the following few years. Those with lesser sensitivity to tuberculin on entry had consistently lower rates than those in the negative unvaccinated group, suggesting that they had some degree of protection against fresh infection, though not as great as that in the vaccinated groups.

In assessing the benefit that would have accrued to the entire trial population from the use of vaccine for *all* those tuberculin negative on entry, the contribution to the total tuberculosis morbidity made by those initially tuberculin positive (and therefore ineligible for vaccination) had to be included. This benefit—that is, the percentage reduction in incidence of tuberculosis during the five-year period—was 59% for B.C.G. vaccine and 61% for vole bacillus vaccine.

In all, 125 participants died from causes other than tuberculosis within five years of entry to the trial. In addition 151 cases, when submitted to the assessor, were classified by him as not due to tuberculosis, these consisting mainly of other chest diseases submitted because the radiographic abnormality persisted for more than 14 days. The incidence of these non-tuberculous deaths and diseases in the five trial groups reveals no significant evidence of protection by B.C.G. or vole bacillus vaccination against any specific cause of death, nor against any chest disease other than tuberculosis.

The trial is still in progress, and later reports will contain more detailed analyses over longer periods of time.

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ELECTROENCEPHALOGRAPHIC STUDIES IN RESPIRATORY FAILURE

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In recent years acute or subacute respiratory failure has been added to the long list of diseases in which there is disorder of mental and nervous function from a primarily extraneural cause. The major changes in this state are known to be hypoxia, hypercarbia, and acidosis of respiratory origin.

Imperfect oxygenation of pulmonary venous blood, with a fall in arterial oxygen tension and saturation, is easily produced by alterations in the relative distribution of inspired gas or pulmonary blood flow. Later, when total effective alveolar ventilation is reduced, carbon dioxide elimination progressively fails, with consequent respiratory acidosis, and below critical levels the clinical syndrome of carbon dioxide retention appears. The manifestations of this syndrome are now well recorded (Donald, 1949; Westlake, Simpson and Kaye, 1955; Sieker and Hickam, 1956). The salient features are headache, confusion, drowsiness, flapping tremor, like that of liver disease, muscular twitching, and coma. It is accompanied by an increase of cerebral blood flow caused by the high arterial carbon dioxide levels (Kety and Schmidt, 1948; Patterson, Heyman, and Duke, 1952), which also cause a rise in C.S.F. pressure (Davies and Mackinnon, 1949). If papilloedema then develops, as it may, cerebral tumour may be mimicked (Cameron, 1933; Leggat, 1958; Conn, Dunn, Newman, and Belkin, 1957).

The effects of giving oxygen when carbon dioxide retention is established are well known (Davies and Mackinnon, 1949; Donald, 1949). Its administration removes the anoxic stimulus to respiration and so results in further decline in alveolar ventilation, which is already defective. There is a further rise in alveolar and arterial carbon dioxide tension with clinical deterioration and coma in some cases.

Although these aspects of respiratory failure have been closely studied, little attention has been devoted to the E.E.G., which might be expected to reflect alterations in cerebral physiology. In an attempt to define the E.E.G. changes, and the conditions under which they occur, we have studied 16 patients on 19 occasions during 18 hospital admissions for acute or subacute pulmonary insufficiency with carbon dioxide retention, and with or without congestive heart failure. Clinical data are presented in Table I. Blood gas studies were made at varying stages in the first two weeks after admission, with one exception when they were made late in convalescence. It was possible to repeat the studies in only one patient during the same hospital admission, but in two patients they were repeated on a second admission. In every case arterial blood gas studies and the E.E.G. were made on the same day and in most cases simultaneously.

TABLE I.—*Clinical Data*

Case No.	Age and Sex	Diagnosis	History of Chest Disease (Years)	History of "Acute" Illness (Days)	Cardiac Failure	B.P.	*X*-ray Findings	E.C.G. Findings	Duration of Admission (Days)	Result	Time of Study*	Mental Symptoms	E.E.G. Abnormality	Notes
1	46 M	Chronic bronchitis	3½	9	No	120/90	Ht.+ R.V.+ Congestion+	S.R. R.B.B.B.	24	Died	1	Confusion. Tremor. Headache	Moderate	Same patient as Case 12; 2nd admission
2	57 F	Asthma. Chronic bronchitis. Emphysema	20	7	Yes	120/80	Ht.+ R.V.+ Congestion+	S.R. R.A.D. P. pulmonale	53	Discharged ambulant	1	Tremor	Mild	Same patient as Case 8; 1st admission
3	73 F	Kyphoscoliosis. Bronchitis. Old myocard. infarct	3	90	,,	185/90	Ht.++ R.V.++ Emphysema+ Kyphoscoliosis	A.F. Old infarct	55	Died	2	Confusion. Drowsy. Headache	Moderate	Previous myocardial infarct 3 years
4	61 M	Bronchitis. Emphysema. Pulmonary fibrosis	20	10	,,	160/80	Ht.++ R.V.++ Fibrosis+	S.R.	20	Discharged ambulant	2	Coma in O_2. Confused. Tremor. Headache	Severe	
5	72 F	Bronchitis. Emphysema. Fibrosis	12	7	,,	170/90	Ht.++ R.V.+ Basal reticulation	S.R. V.E.S.	49	,,	3	Confused	Moderate	1 previous admission
6	58 M	Chronic bronchitis. Emphysema	10	56	,,	170/120	Emphysema	S.R. L.A.D.	23	,,	3	Confused. Tremor	Mild	
7	57 M	Chronic bronchitis. Emphysema. Fibrosis	10	14	No	130/90	Ht.+ R.V.+ Congestion+ Reticulation rt. base	S.R. A.E.S. R.A.D.	75	,,	4	Coma in O_2. Confused. Tremor. Headache	Severe	
8	57 F	Asthma. Chronic bronchitis. Emphysema	20	14	,,	120/70	Ht.+ R.V.+ Congestion+ Emphysema	S.R. R.A.D. P. pulmonale	50	,,	4	Drowsy	Moderate	Same patient as Case 2; 2nd admission
9	59 M	Bronchitis	2	42	,,	190/115	Ht.+ L.V.+ Emphysema	S.R. Ischaemic changes L.V.	14	,,	4	Confused. Headache	,,	Hypertensive. Small cerebral thrombosis 1 year prev. No residual paralysis
10	49 M	Chronic bronchitis. Emphysema	5	42	Yes	140/90	Ht.+ R.V.+ Congestion+ Emphysema Reticulation	S.R. R.V.+	16	,,	5	Headache. Drowsy	,,	
11	53 M	,, ,,	9	29	No	150/115	Ht.++ R.V.+ Congestion+ Emphysema	S.R. R.V.+	25	Discharged bedridden	6	Headache	,,	Hypertensive. 3 previous admissions
12	46 M	,, ,,	3	19	,,	120/60	Ht.+ R.V.+ Emphysema+	S.R. R.B.B.B.	19	Discharged ambulant	7	Coma in O_2. Drowsy. Headache. Tremor	,,	Same patient as Case 1; 1st admission
13	54 M	,, ,,	7	84	,,	140/90	Emphysema	Not done	12	,,	9	None	Mild	Admitted for investn. of headache, but this had gone by time of exam.
14	56 M	Bronchitis. Emphysema	5	28	Yes	170/120	Ht.+ Congestion+ Emphysema	S.R. R.V.+ P. pulmonale	40	,,	9	Drowsy. Confused. Tremor. Paranoid	Moderate	Hypertensive. Same patient as Case 19
15	48 F	Bronchiectasis. Emphysema. P. fibrosis	44	30	,,	110/70	Ht.+ R.V.+ Congestion+ Fibrosis+	S.R. R.V.+	28	Died	10	Tremor. Headache	,,	2 previous admissions
16	66 M	Chronic bronchitis. Emphysema	3	12	,,	170/110	Ht.+ R.V.+ Congestion+ Emphysema	S.R. R.V.+	18	,,	11	Confused. Tremor	,,	Hypertensive
17	52 M	,, ,,	16	40	,,	170/110	Ht.+ R.V.+ Patchy consolidation Effusion Right	S.R. R.A.D.	56	Discharged ambulant	12	Headache. Drowsy. Confused. Tremor	Severe	2 previous admissions. Hypertensive
18	46 F	Bronchiectasis. Emphysema	44	14	,,	130/70	Ht.+ RV.+ Cystic bronchiectasis+ Emphysema	S.R. R.A.D.	33	,,	32	None	Normal	4 previous admissions
19	56 M	Bronchitis. Emphysema	5	28	No	160/115	Emphysema	S.R. R.V.+ P. pulmonale	40	,,	39	,,	Mild	Same patient as Case 14. Day before discharge

X-ray findings: Ht.=Heart. R.V.=Right ventricle. L.V.=Left ventricle. E.C.G. findings: S.R.=Sinus rhythm. A.F.=Auricular fibrillation. A.E.S.=Auricular extrasystoles. V.E.S.=Ventricular extrasystoles. R.A.D.=Right axis deviation. L.A.D.=Left axis deviation. R.B.B.B.=Right bundle-branch block. +, slight abnormality; ++, moderate abnormality; +++, gross abnormality. * Days after admission.

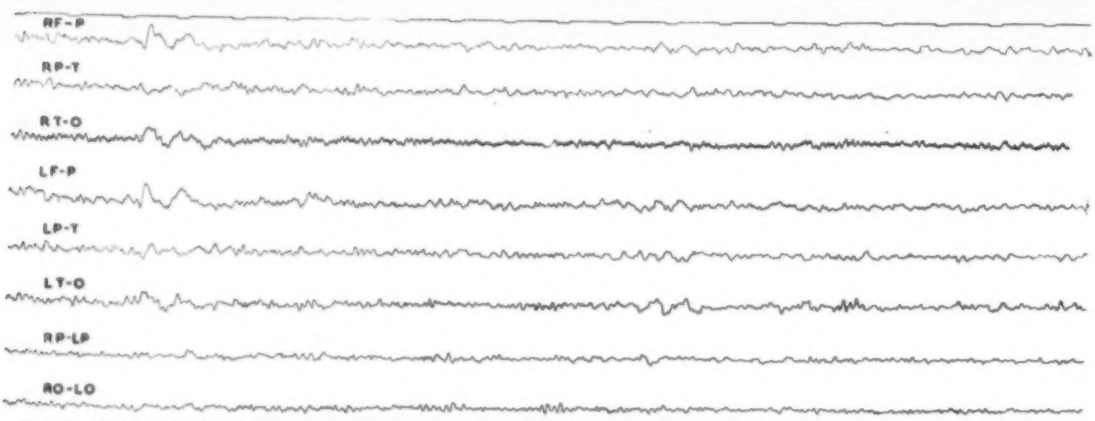

FIG. 1.—High-amplitude delta bursts appear in both cerebral hemispheres at intervals of 10 to 15 seconds. Moderate-amplitude theta activity is also present in all channels and unsustained alpha rhythm can be seen.

Methods

Arterial blood was obtained from an indwelling brachial artery needle and was analysed for carbon dioxide (pCO_2) and oxygen (pO_2) tensions by the bubble method of Riley, Proemmel, and Franke (1945) as modified by Riley, Campbell, and Shepard (1957), using personally established correction factors. Arterial whole blood CO_2 content was determined by the method of Van Slyke and Neill, and plasma CO_2 was estimated from this value, using the nomogram of Van Slyke and Sendroy (1928). The oxygen capacity was measured spectrophotometrically; arterial *p*H was calculated from the pCO_2 and plasma CO_2 content, using the Henderson–Hesselbach equation with a *p*K of 6.11. Serum electrolytes were determined by flame photometry, and serum urea and haemoglobin by standard methods in current use at this hospital.

The E.E.G.s were recorded on a Marconi eight-channel instrument using either standard 10/20 electrode placements or a simpler arrangement often used in this hospital for restless and uncooperative patients. The electrodes were silver/silver-chloride with gauze pads soaked in 5% sodium chloride. All recordings were bipolar, and a standard gain of 0.5 cm. to 50 μV was employed.

Results

The E.E.G. tracings have been classified into four groups: normal, mildly abnormal, moderately abnormal, and severely abnormal. They have been regarded as mildly abnormal if low-amplitude theta activity is intermittently seen temporo-centrally; as moderately abnormal if theta frequencies are more prominent—that is, of higher amplitude, greater persistence, and wider diffusion; and severely abnormal if, in addition to theta activity, delta activity is present. In severely abnormal tracings the delta waves tend to be paroxysmal and of high amplitude, and may occur in bursts which are repeated at fairly regular intervals (Fig. 1). In all the abnormal records the dysrhythmias have appeared in exactly symmetrical positions, and signs of focus or clear unilateral preponderance have been absent. In a number, random sharp waves without fixed location have also been a feature. Oxygen (100% O_2 at 5 l./min.) was given for 15 minutes to seven patients during recording, but no change in the appearance of the E.E.G. resulted, though in each case the arterial pO_2 rose to above normal levels (Table II), and in the five cases in which it changed the pCO_2 rose by a mean of 11 mm. Hg. Only one of our records was normal; four were mildly abnormal, 11 moderately abnormal, and three severely abnormal.

With the use of the degree of E.E.G. dysrhythmia to subdivide the patients, our data show that increasing E.E.G. abnormality is accompanied by a rise in the mean arterial pCO_2 and plasma CO_2 levels and by a fall in the mean arterial pO_2. No distinct trend in arterial

TABLE II.—*Blood Studies*

Case No.	E.E.G. Grade	Hb g./100 ml.	At Rest off O_2 30 min.			On O_2 15 min.			mEq/l.			Urea mg./100 ml.
			pO_2 mm. Hg	pCO_2 mm. Hg	CO_2 mEq l.	*p*H	pO_2* mm. Hg	pCO_2 mm. Hg	Na	K	Cl	
1	Moderate	16·7	39	72	40·02	7·352	—	—	134	4·4	105	112
2	Mild	15·5	37	76	38·09	7·301	—	—	130	5·2	101	67
3	Moderate	13·6	34	75	42·74	7·364	129+	87	127	4·5	79	54
4	Severe	13·0	26	83	46·28	7·343	119+	93	127	5·6	93	36
5	Moderate	15·7	61	50	31·30	7·407	—	—	109	3·8	73	36
6	Mild	11·8	68	49	28·36	7·371	144+	59	126	4·7	101	35
7	Severe	17·2	36	92	47·31	7·317	—	—	130	4·6	89	52
8	Moderate	16·0	30	62	28·18	7·259	—	—	136	4·6	101	33
9	,,	13·3	56	47	30·76	7·430	—	—	—	—	—	38
10	,,	14·8	45	62	32·89	7·330	144+	61	134	4·1	93	95
11	,,	14·5	37	74	33·48	7·257	—	—	134	4·9	97	52
12	,,	12·6	47	83	30·06	7·212	135+	91	140	5·1	102	23
13	Mild	14·8	51	63	30·12	7·280	—	—	—	—	—	—
14	Moderate	18·2	30	82	44·35	7·340	148+	102	—	—	—	42
15	,,	11·1	46	76	28·38	7·167	—	—	134	3·7	85	19
16	,,	14·8	31	81	—	—	—	—	135	4·6	92	56
17	Severe	17·2	38	75	40·04	7·324	—	—	136	6·2	96	39
18	Normal	13·2	54	65	30·10	7·258	123+	65	134	3·9	97	37
19	Mild	18·2	65	57	35·66	7·406	—	—	—	—	—	—

* Uncorrected.

*p*H is evident (Table III and Fig. 2). Age does not seem to be a material factor, nor do variations of serum electrolytes, urea, or haemoglobin show any reciprocity with the E.E.G. pattern.

Attempts to find a relation between E.E.G. change and the duration of the acute illness or the length of time after admission of the date of study have been unsuccessful. The three patients with severe abnormality were discharged ambulant. Four patients died.

Comparison of E.E.G. tracings with mental and physical neurological signs reveals a definite interconnexion (Fig. 3). The more severe the E.E.G. disorder the more likely is the presence of florid clinical manifestations.

Discussion

The E.E.G. changes we have observed in this group of patients correspond with those reported previously by Austen, Carmichael, and Adams (1957) and by Wilson and Sieker (1958). The mild and moderate grades of dysrhythmia do not show any pathognomonic signs, and whilst the occurrence of bursts of high-voltage bilateral synchronous delta discharge can be striking in severe grades, this, too, is a non-specific sign. A similar E.E.G. pattern is a common feature of confusional states of metabolic origin, most notably in hepatic coma but sometimes in uraemia and insulin overdosage, and we have also seen it occasionally with hypercalcaemia and in hypertensive encephalopathy. It should be mentioned, however, that the high-amplitude triphasic complexes described by Bickford and Butt (1955) as a special characteristic of hepatic encephalopathy were not seen.

Though our data demonstrate a link between the degree of E.E.G. abnormality and the severity of hypercarbia and hypoxia, there is no clear connexion between them in individual cases. Indeed, our solitary patient with a normal record had a grossly abnormal arterial pCO_2 and considerable acidosis and hypoxia (Case 18, Tables I and II). This phenomenon compares with our previous experience and that of others (Westlake *et al.*, 1955; Sieker and Hickam, 1956) that the presence of mental and other neurological symptoms does not tie closely with the individual arterial blood gas figures.

The absence of correlation in our patients between arterial *p*H and E.E.G. appearance is interesting, since other writers have stressed that neurological symptoms in pulmonary insufficiency may be related to *p*H fall as

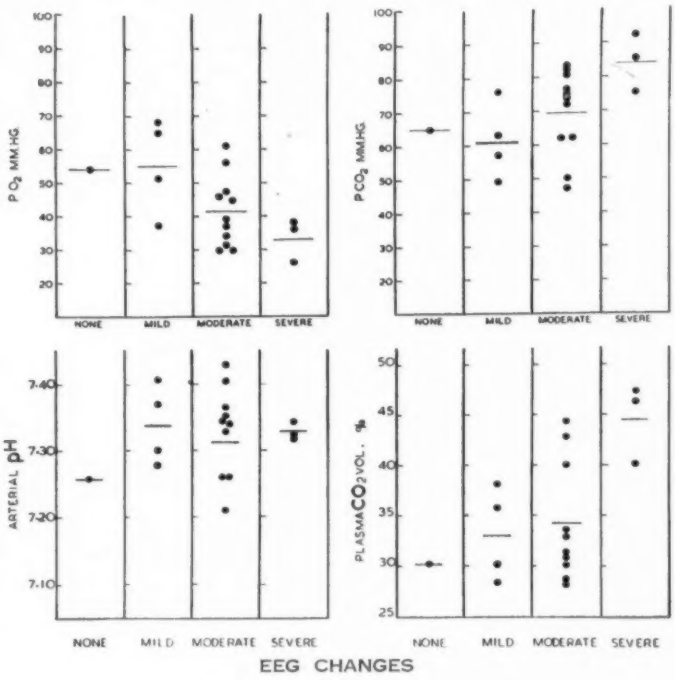

FIG. 2.—Blood gas E.E.G. relationships (arterial blood).

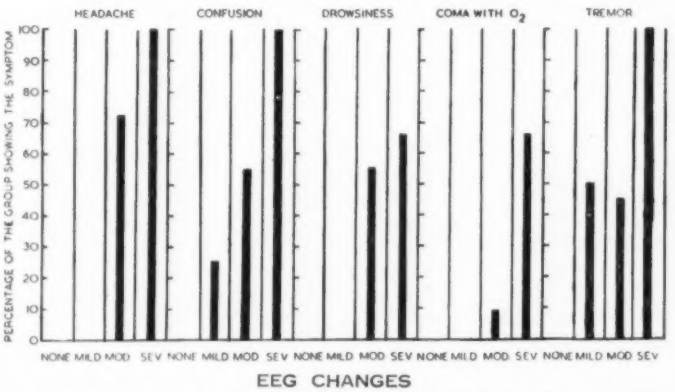

FIG. 3.—The proportion of patients with mental symptoms within the four groups of E.E.G. changes.

TABLE III.—*Mean Blood Values According to E.E.G. Group*

Group (No. of Patients)	Mean Age Years	Hb g./100 ml.	pO_2 mm. Hg	pCO_2 mm. Hg	Plasma CO_2 mEq/l.	*p*H	Serum Values mEq/l.			Urea mg./100 ml.	Individual Day of Study After Admission
							Na	K	Cl		
Normal E.E.G. (1)	46	13·2	54	65	30·1	7·26	134	3·9	97	37	32
Mildly abnormal E.E.G. (4)	56	15·1	55	61	33·06	7·338	128	5·0	101	51	1, 4, 9, 39
Moderately abnormal E.E.G. (11)	57	14·8	41·5	69·5	34·22	7·312	131	4·4	92	51	1, 2, 3, 4, 4, 5, 6, 7, 9, 10, 11
Severely abnormal E.E.G. (3)	57	15·8	33	84	44·54	7·328	128	5·5	93	42	2, 4, 12
Mean values all cases	56	14·9	44	70	38·33	7·318	131	4·7	94	49	

distinct from arterial pCO_2 rise (Westlake *et al.*, 1955). The work of Swanson, Stavney, and Plum (1958) bears on this point in support of our findings, as they have shown experimentally that acute changes in arterial *p*H affect the cats' E.E.G. only when there is an accompanying rise or fall in blood CO_2 tension.

It has been claimed by Wilson and Sieker (1958) that age is important in determining E.E.G. dysrhythmia in respiratory insufficiency, but our results do not demonstrate this. Failure to observe any change in the E.E.G. from inhalation of oxygen during recording is in agreement with similar lack of effect mentioned by others (Brazier quoted by Austen *et al.*, 1957; Wilson and Sieker, 1958).

The immediate causal mechanism of E.E.G. disorder from impaired respiratory function presumably lies in hypercapnia and hypoxia, and our data do not allow choice of which is the more important factor. Though there may be more remote metabolic changes, such as alteration in intracellular electrolyte concentrations, which have an effect on cerebral neuronal activity, our observations, unlike those of Wilson and Sieker (1958), do not disclose any consistent abnormality of serum electrolytes in relation to E.E.G. appearances. This fact must, however, be treated with reserve, as it is generally appreciated that the electrolyte levels of the circulating blood, and in particular potassium, are not a reliable index of ionic levels within tissue cells.

Lastly, we would suggest that the variability of development of E.E.G. disorder in patients with respiratory insufficiency must predicate a great range in individual cerebral homoeostasis in the face of alterations of blood gas levels. In some instances the tolerance of the central nervous system against disturbance by this means must be high and in others relatively low, and the unpredictable behaviour of neural and mental signs and symptoms, *vis à vis* pO_2 and pCO_2 values, can be interpreted in the same light. Our studies satisfy us that there is a close interrelation between neurological semeiology clinically and the presence of E.E.G. dysrhythmia—a closer nexus than exists between either of these phenomena and the arterial oxygen and carbon dioxide tensions.

Summary

Sixteen patients have been studied during 18 hospital admissions for acute or subacute respiratory failure. The E.E.G., clinical signs and symptoms in the nervous system, and blood gas findings have been compared.

The E.E.G. shows symmetrical changes from intermittent theta activity to paroxysmal delta discharge of high amplitude, and the changes resemble those found in other types of confusional state, particularly those of metabolic origin.

There is good correlation between the E.E.G. abnormality and the clinical neurological findings. There is also a correlation between increasing E.E.G. abnormality and a falling pO_2 and rising pCO_2 and plasma CO_2 content when the patients are considered as groups, but not in individual cases. No relationship with arterial *p*H was observed. No other relationships were noted.

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SYPHILIS AS A CAUSE OF MENTAL DEFICIENCY

BY

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Figures derived from the Ministry of Health (1958) report for 1957 illustrate the fact that syphilis is becoming increasingly rare in England and Wales (Tables I–III).

TABLE I.—*Cases of Syphilis Dealt With at Centres in England and Wales*

Year	No. of Cases, in all Stages, Dealt with for First Time	No. of Cases of Acquired Syphilis with Infections of Less than One Year
1931	—	8,924
1939	11,878	4,986
1946	23,878	17,675
1952	7,122	1,353
1957	4,977	747

1946 was the post-war peak year. The dramatic decline in the disease is indicated by the fall in attendances to a record low level 11 years later.

Lest it be thought that modern methods of treatment obscure the true incidence of syphilis, the figures in Table II demonstrate that general paralysis of the insane, one of the main late clinical forms of the disease, is now much less important than it was.

TABLE II.—*Deaths from General Paralysis of the Insane in England and Wales*

Years	No. of Deaths
1911–20	2,080*
1936–9	852*
1945–9	359*
1953	117
1957	68

* Average annual deaths.

The decline in acquired syphilis has been paralleled by a similar change in the incidence of the congenital disease, as shown in Table III. In this case the peak of the relatively small wartime rise was reached in 1943, with a steady decline thereafter.

Routine serological tests for syphilis on pregnant women at various regional blood transfusion centres in England during 1957 showed a percentage incidence of

TABLE III.—*Congenital Syphilis in England and Wales*

Year	Cases Dealt with for First Time at Treatment Centres	Death Rates per 1,000 Live Births of Infants under 1 Year, Certified as due to Congenital Syphilis
1931	2,439	0·45
1939	1,614	0·17
1943	1,727	0·23
1950	1,223	0·04
1957	557	Nil

positives of 0.14% for primiparae and 0.29% for multiparae. The equivalent figures for 1953 were 0.21% and 0.43% (Ministry of Health, 1958).

With the fall in the incidence of syphilis in this country, mental deficiency due to it should become correspondingly less common and may eventually disappear from clinical practice.

Syphilis and Mental Defect

For practical purposes, syphilis as a cause of mental defect may be considered under the head of congenital syphilis. Legally, mental deficiency is defined as "arrested or incomplete development of mind existing before the age of 18 years." Occasionally, a 13- or 14-year-old child may acquire syphilis and develop general paralysis before the age of 18, but this must be a rare event. Most cases of syphilis producing mental defect are derived from the mother and are congenital.

In assessing the role of syphilis as a cause of mental defect it is important to exclude cases of acquired syphilis amongst adults previously mentally retarded. One reason for sending feebleminded women to institutions was, and to some extent still is, the fact of illegitimate pregnancy, prostitution, or promiscuity. In this way there might be a tendency to collect in institutions for mental defectives a group at special risk in regard to acquired syphilis.

A further difficulty arises in regard to diagnostic criteria. Some of the earlier writers were inclined to look upon syphilis as an aspect of "moral degeneracy" rather than as a disease entity, and this may have resulted in increased estimates of the amount of mental deficiency due to the condition. Matters improved with the introduction of the Wassermann reaction into general use prior to the first world war, though technical errors were not infrequent. A refinement has been the development of various parallel tests, though even now the clinician is all too ready to base a diagnosis of syphilis on a single laboratory report. In our experience, it is not uncommon for a single positive report to be followed by several negative ones, and this experience extends over a great number of laboratories.

An additional consideration is that, even though the existence of syphilis in the mother be proved, it does not necessarily follow that any mental defect in the child is of syphilitic origin. A final possibility to be considered is the coexistence in the defective child of congenital syphilis and some other anomaly which might be responsible for the defect.

Tredgold (1929) reviewed some of the earlier literature on the role of syphilis in mental defect, and expressed his own opinion that "investigation of family histories would lead to the conclusion that syphilis was not a frequent cause of amentia." In his own series, 2.5% presented "undoubted marks" of the disease. He quotes serological investigations, carried out before the first world war, which gave an incidence varying from 1.5% to 44.9% of positive Wassermann reactions in mental defectives. As recently as 1926, Stewart found 158 positive reactions in 800 mental defectives (19.75%) in Leavesden Hospital. This contrasts with 57 positives amongst 1,631 defectives (3.4%) at the Wrentham State School, Massachusetts (Dayton, 1925). In 1931 Cobb (quoted by Penrose, 1954) found positive serological tests in 129 of 1,275 cases (10.1%).

In the Colchester survey (Penrose, 1938), 51 patients out of 1,280 (4%) were diagnosed as having congenital syphilis, and 41 of them had positive blood Wassermann reactions. Penrose's figure of 4% is identical with that of Benda (1942), who found definite evidence of congenital syphilis in 80 of 2,000 patients of all ages at the Wrentham State School. In contrast to this is Paddle's (1937) finding of 10% for the incidence of congenital syphilis amongst the children at Caterham Hospital.

Syphilis, like rubella, is one of the few diseases in which there is good evidence that maternal infection during pregnancy may damage the infant. The risk is high, and it has been estimated (Moore, 1941) that a woman with latent syphilis has only one chance in six of bearing a normal child if she is untreated. Transmission of infection to the infant probably does not occur till the fifth month of pregnancy, which gives a period of grace during which infections discovered by routine antenatal serological investigation can be treated. Infections acquired later in pregnancy constitute a great danger, however.

Earlier views on the role of syphilis in producing mental deficiency were that it acted on the parental germ plasm; that the disease affected the general health of the mother and hence that of the foetus; that the disease produced mental defect only when there was a "neuropathic taint"; and that simple idiocy, without specific evidence of syphilitic lesions, might be due to the disease. The tendency to regard both mental deficiency and syphilis as punishment for sin is exemplified by Shuttleworth and Potts (1922), who state: ". . . a solitary infraction of physiological law is not often followed by the penalty of mental abnormality; if we only look far enough we shall generally find that such a culmination is reached by repeated transgressions." These authors also quote work suggesting that syphilis is responsible for 50% of cases of epilepsy as well as a considerable proportion of cases of mental defect showing neither "stigmata" nor any evidence of gross lesions in the central nervous system.

It is now generally agreed that congenital syphilis produces mental deficiency by spirochaetal invasion of the nervous system, and that the clinical syndromes resulting from this invasion can be classified in a similar manner to those which are found in the acquired disease. The main groupings are general paralysis with or without tabes, and meningovascular syphilis. There is no evidence to suggest that any other clinical types of mental defect are due to syphilis.

Incidence and Classification of Syphilis in Present Series

The Fountain Hospital Group provides accommodation for 800 mental defectives, mainly from the London area. Of these, about 80% are children of idiot or imbecile level, the majority of the remaining 20% being feebleminded adults. A specimen

TABLE IV.—*Findings in Six Mental Defectives with Congenital Syphilis (Two other Cases (Cases 4 and 5) are Reported Fully in the Text)*

	Case 1	Case 2	Case 3	Case 6	Case 7	Case 8
Date of birth	1/2/08	5/10/25	14/5/33	15/12/44	13/11/45	20/1/47
Birth weight	?	?	?	5 lb. 3 oz. (2,354 g.)	5 lb. (2,268 g.)	5 lb. (2,268 g.)
Sex	Female	Female	Female	Female	Male	Male
Status	Illegitimate	Illegitimate	Illegitimate	Illegitimate	Legitimate	Legitimate
Mother: Syphilitic history	Attended V.D. clinic 16 years after patient's birth. Treated with arsenicals and mercurials	Syphilis diagnosed 10 years after patient's birth. Incompletely treated	? Syphilitic	Blood W.R. and Kahn positive and rash when 7 months pregnant. Condylomata of anus and vulva at delivery. Treated antenatally	? Syphilitic	G.P.I. diagnosed 4 years before patient's birth. Treated with fever therapy and penicillin. Blood W.R. positive post-natally. Treated with penicillin, bismuth, and arsenicals
Mother: Other pregnancies	8 previous pregnancies (3 miscarriages; 4 stillbirths) and 8 subsequent ones (4 miscarriages)	5 previous children (4 illegitimate; 2 died in infancy). No miscarriages or stillbirths	Previous miscarriage. No stillbirths	3 subsequent normal pregnancies. No miscarriages or stillbirths	Previous illegitimate macerated stillbirth. Previous illegitimate premature child who died at 3 weeks	Previous stillbirth. Previous congenital syphilitic who died in infancy
Father	Nothing known	Nothing known	Nothing known	Nothing known	? Syphilitic. 6 children by former marriage 1 died in infancy; others normal	Treated for syphilis
Patient's progress: Syphilitic history	.. ..	Syph. periostitis of tibia and positive blood W.R. and Kahn at 7 years. Irregular treatment with bismuth, arsenicals, and mercurials for 6 years	.. ..	Blood W.R. and Kahn positive at birth. Treated with bismuth and arsenicals. Considered cured at 2 years	Cord blood W.R. positive. At 3½ years blood W.R. and Kahn positive. C.S.F., Lange paretic and excess proteins. Partially blind; optic atrophy; choroiditis; rhagades; snuffles. Treated with penicillin	"Poor specimen" at birth. Syphilitic. Treated with penicillin, bismuth, and arsenicals. No clinical or serological evidence of syphilis at 2 years
Patient's progress: Other features	Walked at 2 years. Went to school for defectives at 7 years	? Early development normal. Attended special school from 12–14 years. Many jobs and theft charge later	Retarded from infancy	Ophthalmia neonatorum at birth. Retardation and nystagmus at 8 months. Blind at 16 months	Retarded from infancy	Retarded from infancy. Fits for first 2 years of life
Findings on admission to Fountain Hospital						
Age (years)	15½	23½	3½	6 2/12	11½	5 2/12
I.Q.	? (Imbecile)	82	29	35	60	24
Height	62 in. (157·5 cm.)	62 in. (157·5 cm.)	32 in. (81 cm.)	39½ in. (100 cm.)	51 in. (129·5 cm.)	36 in. (91·5 cm.)
Weight	62½ lb. (28·3 kg.)	128 lb. (58·1 kg.)	32 lb. (14·5 kg.)	33½ lb. (15·2 kg.)	51 lb. (23·1 kg.)	37 lb. (16·8 kg.)
Serology	?	Blood W.R. and parallel test negative	Blood W.R. and Meinicke positive. C.S.F. normal	Blood W.R., Kolmer, and Meinicke negative	Blood W.R. negative. C.S.F. normal	Blood and C.S.F. normal
Clinical findings	Hemiparesis. Choroiditis. Strabismus	? Frontal bossing	Psychotic features	Blind. Optic atrophy. Nystagmus	Partially blind. Optic atrophy. Choroiditis. Peg-shaped teeth	Strabismus
Subsequent developments	Blood W.R. and Meinicke often positive from 24 to 39 years. C.S.F. W.R. positive and Lange paretic at 26 years. Treated with arsenicals. Employed in community from 36 years	Able to manage own affairs at 26 years	Blood W.R. and Meinicke positive till 14 years. Treated with arsenicals for 2 years. Subluxation of femoral epiphysis at 16½ years. Mentally unchanged at 18 years	C.S.F. W.R. negative at 14 years. I.Q. then 50	Discharged at 12 years with recommendation for admission to school for educationally subnormal	No significant progress in next 6 years

TABLE V.—*Findings in Four Mental Defectives with Maternal History of Syphilis*

	Case 9	Case 10	Case 11	Case 12
Date of birth	25/5/44	9/7/48	7/2/50	2/7/50
Birth weight	10 lb. 7 oz. (4,735 g.)	8 lb. 8 oz. (3,855 g.)	6 lb. 5 oz. (2,865 g.)	9 lb. 7 oz. (4,280 g.)
Sex	Female	Male	Female	Female
Status	Illegitimate	Illegitimate	Illegitimate	Legitimate
Mother: Syphilitic history	Syphilis diagnosed 2 years before patient's birth. Irregular treatment for 2 years	Syphilis diagnosed at 38th week of pregnancy. Treated with bismuth and arsenicals	Blood W.R. and Kahn positive twice after labour. Treated with penicillin post-natally	Blood W.R. and Kahn positive 2 years after patient's birth. Treated with penicillin without effect on serology
Mother: Other pregnancies	1 previous child, 2 subsequent children, all healthy. No miscarriages or stillbirths	Nothing	Nothing	2 subsequent children, normal. 1 subsequent stillbirth
Father	"Healthy"	Nothing abnormal known	Nothing known	No evidence of syphilis
Patient's progress	? Normal development till lens opacities and partial blindness noted at 15 months	? Normal early development	Normal development till head injury at 11 months	Retarded from infancy
Findings on admission to Fountain Hospital				
Age (years)	9½	3 1/12	1 11/12	4 1/12
I.Q.	20	49	26	37
Height	?	37 in. (94 cm.)	34 in. (86 cm.)	36 in. (91·5 cm.)
Weight	78½ lb. (35·6 kg.)	35½ lb. (16·1 kg.)	23¾ lb. (10·8 kg.)	36 lb. (16·3 kg.)
Serology	Blood W.R. and Kahn negative	Blood W.R. and Meinicke negative. C.S.F. normal	Blood W.R. and Meinicke negative. C.S.F. normal	Blood W.R. and Kahn negative
Clinical findings	Blind. Emotionally disturbed	Nothing abnormal found	Petit mal. Ptosis. Hemiparesis. Extensor plantars. Ankle clonus	Epilepsy. Strabismus

of blood is taken routinely on admission for Wassermann and parallel tests. Should either be posititve, a second specimen is sent for examination. If the serum tests are consistently positive the cerebrospinal fluid is then examined. Data have been accumulated over a 12-year period, 1947–58, during which time some 1,900 patients have been available for examination. A note has been made of cases where serum tests were consistently positive, where there were clinical signs of syphilis, and where there was a history of syphilis in the patient or his mother.

A total of 12 patients fell into one or more of these categories, so that there was a prima facie case for consideration of syphilis as the cause of their mental deficiency. In seven of these patients there was convincing evidence of congenital syphilis. In an eighth case the evidence was a little less clear-cut but was acceptable. In the remaining four children there was a history of maternal syphilis but no reliable evidence that the child was suffering from the disease. Details of six of the eight cases with congenital syphilis are summarized in Table IV—the other two being reported in full below—and of the four with maternal syphilis in Table V. It is notable that 4 of our 12 patients were born before the second world war and none after 1950. Also of interest is the fact that 7 of the 12 were illegitimate.

Without the support of neuropathological material it is difficult to make a precise diagnosis in some mental defectives with congenital syphilis. Table VI shows a tentative grouping of our cases.

TABLE VI.—*Clinical Classification of 12 Mental Defectives with Syphilitic History*

Form of Syphilis	No. of Cases	Case No.
Taboparesis	3	4 certain; 6 and 7 probable
Meningovascular	2	1 and 5
Congenital with mental defect	3	2, 3, and 8
Maternal only	4	9, 10, 11, and 12

There was only one classical taboparetic (Case 4), but the association of mental defect with congenital syphilis in Cases 6 and 7 (optic atrophy in Case 6, and positive cerebrospinal fluid findings in Case 7) was thought to justify their inclusion in this group. The two patients with hemiparesis (Cases 1 and 5) were thought to have the meningovascular form of the disease with a localized lesion. The remaining three cases in which congenital syphilis was regarded as established (Cases 2, 3, and 8) may or may not owe their mental deficiency to the disease. There is no good evidence in Cases 2 and 3 to suggest that the nervous system was ever invaded. In Case 8 the history of fits in infancy and treatment including penicillin is compatible with an early neurological lesion which may have been arrested by treatment, leaving the blood and cerebrospinal fluid normal.

Finally, there is the group of four cases with syphilis in the mother but no evidence of infection in the infant. There is no sound basis for considering that these children are mentally defective because of syphilis. On the other hand, the possibility cannot be completely dismissed. For example, in Case 10 treatment was started at the 38th week of pregnancy. It seems just possible that treatment may have arrested disease in the infant's already damaged brain but left it free from clinical signs of infection.

In this series there is not sufficient information about the precise date of the mother's infection to attempt to draw conclusions from this. It is usually thought that neurosyphilis in the infant is more likely to occur in the later stages of the maternal infection. It will be seen that a number of the mothers had had previous miscarriages, stillbirths, or children who died young, including one known to be syphilitic.

Case 4

This patient, a girl, was born on September 28, 1936. No history of parental syphilis was elicited, but the parents were regarded as very unreliable witnesses. The mother had a stillbirth prior to the patient's birth, and, following the latter, four apparently normal children with no further stillbirths or miscarriages.

The patient weighed 9 lb. (4,080 g.) at birth. Details about the earlier years of life are not known, but there is a suggestion of normal development till the age of 7. At 9 years she was admitted to hospital because of fits and found to be mentally retarded. Argyll Robertson pupils, tremor of the tongue, and slurred speech were noted. The knee- and ankle-jerks were absent. Plantar responses were flexor and the gait was steady. No other clinical abnormalities were found. The blood Wassermann reaction was positive and the cerebrospinal fluid revealed a positive Wassermann reaction, a colloidal gold (Lange) curve of 5555543200, 36 cells per c.mm., and a protein content of 90 mg. per 100 ml. Cerebrospinal fluid examination six months later, after intrathecal and intramuscular penicillin, yielded a positive Wassermann reaction, a negative Lange curve, 5 cells per c.mm., and a protein content of 100 mg. per 100 ml. Before further investigations and treatment could be undertaken, the mother insisted on taking the patient home.

The child was admitted to the Fountain Hospital when 11¼ years old. Her height was 4 ft. 11 in. (150 cm.), her weight 96 lb. (43.5 kg.), and her I.Q. 43. She was co-operative and considerate, her habits were clean, and she could feed and dress herself. She answered simple questions but could not spell her name, did not know her age, and suffered from attacks of screaming. She could count to 20 and knew the alphabet to letter F. There were no physical signs apart from slight Rombergism and absent knee-jerks. The blood Wassermann and Meinicke reactions were doubtfully positive, and the cerebrospinal fluid yielded a negative Wassermann reaction, a Lange curve of 0122100000, and a positive Pandy test. At 14 years the cerebrospinal fluid was normal in all respects apart from a Lange curve of 1121000000. Over the next few years there was slight but not significant improvement in her mental level.

Case 5

This patient, an illegitimate male, was born on July 29, 1944. The mother was found to have secondary stage syphilis seven weeks before the child's birth. She was treated with bismuth and arsenicals till her confinement, her blood Wassermann reaction and Kahn test remaining positive throughout. Treatment continued for two weeks after delivery, when she discharged herself from hospital, taking the child with her. She had had an apparently normal child two years previously. No other pregnancies are known. She said that the father had venereal disease.

The child weighed 8½ lb. (3,855 g.) at birth, following a full-term normal delivery. Wassermann reaction and Kahn test on the cord blood were negative, and several days later were again negative; there was no clinical evidence of syphilis neonatally. The child remained with the mother without further medical attention till 8 months old, when he was investigated in hospital after a convulsion. The fit was associated with otitis media and a respiratory infection, and, in addition, craniotabes and positive blood Wassermann reaction and Kahn test were noted. There were no bony

changes on *x*-ray examination. The cerebrospinal fluid showed a positive Wassermann reaction and a colloidal gold (Lange) curve of 11100000 with no excess of protein or cells. Antisyphilitic treatment, consisting of penicillin, bismuth, and arsenicals, was begun at this stage and continued for two and a half years. During this period the blood Wassermann reaction and Kahn test were repeatedly positive and the child was ataxic and mentally defective. When 3 years old he developed a left hemiplegia. Thereafter, several blood and cerebrospinal fluid examinations yielded negative results.

On admission to the Fountain Hospital at the age of 3½ years his I.Q. was 48. His height was 39½ in. (100 cm.) and weight 31 lb. (14 kg.). He was a quiet child with a limited vocabulary, who could feed himself with a spoon, help dress himself, and had sphincter control. He took considerable interest in his surroundings, and could point out parts of his body on request. Physically, the only abnormalities were left hemiparesis with a left extensor plantar response, and internal strabismus of the left eye. No evidence of syphilitic infection was found in the blood or cerebrospinal fluid. He progressed in hospital, and by the age of 11 was well within the educationally subnormal range. He then began attendance at a school for educationally subnormal physically handicapped children.

Discussion

Even if all 12 of our cases owe their defect to congenital syphilis, the incidence in this series is only 0.6%. If more stringent criteria are used, however, only Cases 1, 4, 5, 6, and 7 are acceptable, in that they showed evidence of neurosyphilis in the form of changes in the cerebrospinal fluid, or appropriate clinical signs. This gives a figure of 0.2% due to congenital syphilis. Even the larger of these two percentages is very much lower than many previously reported, and the conclusion is that syphilis is not now a major factor in the London area as a cause of mental deficiency. We have no reason to think that the position in London is not typical for the country as a whole. Table VII shows the relative frequency of syphilis compared with other aetiological factors or syndromes found in our series of 1,900 mental defectives.

TABLE VII.—*Cases Diagnosed in Certain Categories in Fountain Hospital Group, 1947 to 1958.*

Category	No. of Cases
Mongolism	249
Meningitis (tuberculous and purulent)	40*
Phenylketonuria	28
Kernicterus	21
Tuberous sclerosis (epiloia)	15
History of syphilis	12
Rubellar embryopathy	10
Cerebral lipoidosis	8
Sturge-Weber syndrome (naevoid amentia)	4

* Includes six cases where meningitis was of doubtful aetiological significance.

An obvious explanation for a decline in the proportion of mental deficiency due to syphilis is the general decline in the incidence of the disease as shown in the figures given above. The results arrived at in earlier surveys were, however, so variable that we are inclined to believe that many of the higher estimates were unreliable. It is well known that the technical level of the results in different laboratories has varied (Aselmeyer, 1939). An additional factor which may account for some of the reported differences has been mentioned—namely, failure to insist on a repetition of tests before regarding a patient as syphilitic on serological evidence. Despite the conflicting evidence from earlier figures, there is no doubt that there has been a striking and gratifying decline in the number of cases of mental defect due to syphilis over the past 20 years. Penrose's Colchester estimate may be taken as a conservative basis for comparison.

A striking feature of the figures quoted earlier for new cases of acquired syphilis was the big increase during and after the second world war. It might have been anticipated that this would bring about a similar rise in congenital syphilis. It is presumably a tribute to the efficacy of treatment that the rise was relatively small. It may also be that effective treatment of affected infants will have prevented some from developing neurological lesions and hence from becoming mentally defective.

Conclusion and Summary

Congenital syphilis is now rare as a cause of mental deficiency in England and Wales. The rise in the incidence of acquired syphilis associated with the second world war does not seem to have been paralleled with a great increase in congenital syphilis or mental defect due to this cause. This is presumably a result of good antenatal supervision of pregnant women and prompt treatment of acute cases amongst expectant mothers and infants.

There is no good evidence that syphilis produces any forms of mental deficiency other than well-recognized syndromes such as general paralysis and meningovascular syphilis. Syphilitic mental deficiency is eminently preventable and should disappear. So long, however, as the number of adult cases remains at the present still considerable level, it would be unwise to relax precautions like a routine antenatal Wassermann test or routine investigation of admissions to mental deficiency hospitals, with appropriate attention to the families if positive cases are found. Increasing contact with countries which have been less successful in resolving this problem is an additional argument in favour of retaining such precautions.

Among some 1,900 mental defectives, mainly idiot and imbecile children, studied in the Fountain Hospital Group from 1947 to 1958 there were 12 with a history of syphilis. In eight cases there was congenital syphilis—three of these were classified as taboparetic and two as meningovascular, leaving three whose mental defect was not certainly attributable to their congenital syphilis. In the remaining four cases the mother only was affected and there was no proof of infection in the child.

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PRELIMINARY OBSERVATIONS ON PHENETHYLDIGUANIDE

BY

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The alarming toxic effects of "synthalin A" (Bodo and Marks, 1928; Creutzfeldt, 1957) led to its withdrawal from use, although it was pharmacologically promising. The related compound phenethyldiguanide (D.B.I.) has been reported to be totally lacking in toxicity, the only barrier to its use being the high incidence of nausea and vomiting (Krall and Camerini-Davalos, 1957; Pomeranze *et al.*, 1957). While the hepatic output of glucose is reduced, like synthalin, it causes hypoglycaemia in eviscerated animals, and is thus not wholly dependent for its effect on the presence of active beta cells in the pancreas (Frank *et al.*, 1926; Nielsen *et al.*, 1958). It is able to influence peripheral glucose utilization, as shown by muscle culture, an effect which, unlike the sulphonylureas, it shares with insulin (Williams *et al.*, 1957). It was our aim to assess its value in the out-patient treatment of diabetes mellitus.

Choice of Patients and Dosage

Fifty-two patients were selected for their ability to co-operate in urine tests, and, where it applied, in the adjustment of insulin dosage as indicated by the tests. None had evidence of hepatic or renal disease. Ages varied from 12 to 75, and weight was in all cases within 10% of accepted normal standards. Twenty-nine were on insulin and the remainder were freshly diagnosed cases, or those in whom dietary treatment had proved inadequate. Loss of weight, glycosuria, and a blood-sugar level in excess of 200 mg. on three occasions, each two hours after a main meal, was regarded as evidence of this. To prevent confusion through patients dieting carefully only after active tablets were given, placebo tablets were administered in the last two weeks of the preparatory period, and, in fact, eliminated two of the intended subjects by showing that dietary control sufficed. A diet in the region of 170 g. of carbohydrate was given, except to those in vigorous employment, when it was increased appropriately.

Two 25-mg. tablets of D.B.I. were administered daily for the first week of treatment, and this dosage was increased at subsequent weekly or fortnightly visits to a maximum of 200 mg. daily if necessary. Morning and evening urine specimens were examined at the clinic, and a blood sugar estimation was carried out two hours after a main meal. The criteria of control of diabetes were: (*a*) morning and evening urine tests were almost sugar-free; (*b*) blood sugar, two hours after a main meal, was less than 140 mg./100 ml; (*c*) weight was constant; and (*d*) diabetic symptoms were absent.

The successful patients were treated for periods varying from three to six months.

Results (See Table I)

For convenience the patients are divided into four groups: (A) Adult diabetes: patients over 40 in whom insulin requirement did not exceed 40 units daily. (B) Stable juvenile diabetes: judged from absence of acetone and a moderate or mild diabetic glucose-tolerance curve as in group A. (In group A 20 out of 24 were recently diagnosed and had not yet been given insulin; in group B 3 out of 8 were similarly new cases.) (C) Adult diabetes in which insulin dosage exceeds 40 units daily. (D) Juvenile diabetes in which insulin dosage exceeds 40 units daily. It is appreciated that the division is to some extent arbitrary. Adults sensitive to insulin in low dosage with a tendency to acidosis may be concealed in group A, and members of group D will graduate with age into group C. Group A is that which is usually successfully controlled by the sulphonylureas.

TABLE I

Group	No.	Success*	Partial Success†	Failure
A (adult)	24	21 (88%)	1	2
	4 on insulin	2 on insulin		1 on insulin
B (stable juvenile)	8	4 (50%)	3	1
	5 on insulin	1 on insulin		on insulin
C (adult unstable)	13	3	7	3
		28%		
D (juvenile)	7	1	4	2
		14%		
Total	52	29	15	8

* "Success" indicates that insulin was withdrawn, or not required to obtain control.
† Partial success indicates a fall in insulin dosage of more than 20 units.

1. *Successes.*—Although the mode of action of D.B.I. and the sulphonylureas is not identical, the same group (A) was most favourable for treatment with D.B.I. as they would be with the sulphonylureas. 88% of group A diabetics were well controlled by D.B.I., which compares favourably with the anticipated results of treatment with carbutamide or tolbutamide. In two cases the drug apparently had no effect; in one case nausea made use of the drug intolerable. Group B gave a success rate of four in eight cases, and three of those not completely successful showed a fall in insulin dosage of over 20 units. Groups C and D, although differing in age, showed no real variation in their susceptibility to the action of the drug. On the reduced dose, control of diabetes was more accurate as measured by blood sugars, urine tests, and incidence of hypoglycaemia. Of the unstable cases, only three in the older group and one younger patient were controlled without insulin. Those in whom the insulin dose was substantially reduced but not eliminated are regarded as partially successful if urine control was good. The mean duration of treatment of the successful patients was 18 weeks, with a spread of 12 to 24 weeks.

2. *Dosage and Insulin Replacement.*—In 10 patients scattered throughout the four groups, the hypoglycaemic effect was greater in the first week or two, and thereafter the dose of insulin had to be increased substantially before a final control figure was reached. When a substantial effect was found with the initial small doses, further advance did not usually increase the insulin replacement or hypoglycaemic effect. This gave the impression of a threshold of hypoglycaemic action. The effective dose was not predictable from any of the other factors we observed. The dose of D.B.I. used in the successful cases varied. Stable adults were controlled by smaller amounts, the average dose and range being: group A (21), 105 mg. (50–150 mg.); group B (4), 150 mg. (100–200 mg.); group C (3) 167 mg. (100–200 mg.); group D (1), 150 mg. In the partially successful cases the daily dose of D.B.I. was increased to 200 mg. and in

three cases to 300 mg. when nausea was not troublesome. Table II shows the insulin replaced in the four groups.

3. *Appearance of Alimentary Symptoms* (see Table III).—This has been a problem in our series as in others. Fourteen (27%) had nausea and 6 (12%) complained of mouth dryness and discomfort, making a total of 39%. In only 4 cases, one in each group, was nausea the reason for the drug being withdrawn. Its frequency was higher in the stable adult cases, but these tolerated it well probably because it was milder. On the appearance of nausea the dose was reduced by 50 mg. daily and the patient was reminded to take the drug after food; while the appetite was frequently poor for a week or two, it returned to normal and the dose of the drug was cautiously advanced, often beyond the initial amount. Mouth symptoms were transitory in all. The nausea did not coincide with the appearance of acetone. Diarrhoea was met in only one patient, with nausea.

TABLE II

Group	No.	On Insulin	Range of Dose Fall	Mean Fall	Insulin Discontinued In
A	24	4	32–16	22 units	2
B	8	5	36–12	18 ,,	1
C	13	13	40–8	24 ,,	3
D	7	7	32–12	22 ,,	1

TABLE III.—*Side-effects*

Group	No.	Nausea	Mouth Symptoms	Total Alimentary Symptoms	Acetonuria (see Text)
A	24	8	3	11 (46%)	3 (13%)
B	8	2	0	2 (25%)	2 (24%)
C	13	3	3	6 (56%)	3 (28%)
D	7	1	0	1 (14%)	3 (42%)
Total	52	14	6	20	11

4. *Acetone.*—This appeared in 11 cases, and in none of them was it associated with the usual high blood-sugar levels. Six of the cases were in the unstable groups, and 2 of the four Group A cases had shown acetone in the urine before, while under our care. In 4 cases it appeared with hypoglycaemia, and in the others the blood-sugar level varied from 160 to 220 mg./100 ml. (mean 193 mg.). With one exception it disappeared promptly with an increase in the patient's intake of carbohydrate over the planned diet. In this patient acetonuria persisted until the drug was withdrawn. In 5 cases the alkali reserve of plasma was estimated; it was at the lower limit of normal in 3 and approximately 10 volumes/100 ml. below normal in 2. This contrasts with the very low alkali reserve of plasma in pre-coma and is clearly a different entity. In each of these patients weight had fallen from loss of appetite, and starvation ketosis is thought to be the cause.

5. *Toxicity.*—Frequent W.B.C. counts were carried out; also liver function tests (alkaline phosphatase, thymol turbidity, serum bilirubin). In none were the tests abnormal.

6. *Hypoglycaemia.*—In no case did the administration of D.B.I. cause hypoglycaemia when it was not accompanied by insulin.

7. *Comparison with Carbutamide.*—In 12 cases a comparison with carbutamide was possible as the patients were treated with both. It was our impression that carbutamide is less powerful. In Case 7 the usual order was reversed in that D.B.I., although producing normoglycaemia, caused nausea of such a degree as to make the drug intolerable. Carbutamide did not reduce the blood sugar subsequently. In the other cases carbutamide had failed initially for the reasons stated (see Table IV).

TABLE IV

Case No. and Group	Carbutamide	D.B.I.
39 (D)	No effect	No effect
40 (C)	,, ,,	,, ,,
48 (A)	Late failure	,, ,,
41 (C)	,, ,,	Control
44 (A)	,, ,,	,,
38 (A)	Failure with acidosis	,,
46 (C)	,, ,, ,,	,,
49 (C)	No effect	Partial control
21 (C)	,, ,,	,, ,,
22 (D)	,, ,,	,, ,,
52 (C)	,, ,,	,, ,,
7 (A)	,, ,,	Nausea, failure

Summary and Conclusion

In our experience the action of D.B.I. on the adult stable type of diabetes is impressive. Nausea is controlled rapidly by a reduction of dose, and the cases in which it makes treatment impossible are too few to vitiate its value as a hypoglycaemic agent. Unnecessarily high dosage is probably the explanation of the frequent appearance of this symptom in some other series (Hall *et al.*, 1958; Pomeranze *et al.*, 1957). Late failure of control (Williams *et al.*, 1957) did not occur in our group, with one possible exception, although the short period of observation does not allow one to be dogmatic. Ketonuria may develop in the presence of a normal or low blood sugar and is therefore not of the alarming type which usually appears in diabetes. It usually disappears with the use of a high carbohydrate diet and is probably related to starvation ketosis. The striking absence of toxicity indicates that the drug should continue to be used in the adult diabetic, and it may have a place in the treatment of stable juvenile cases also. Like the sulphonylureas, in spite of its different mode of action it is unsuitable for unstable cases if used alone.

D.B.I. appears to control or partially control some cases which do not respond to carbutamide, its hypoglycaemic effect thus being more powerful.

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APPEARANCE OF PARKINSONISM IN MENTALLY DEFECTIVE PATIENTS TREATED WITH "DARTALAN"

WITH THE OCCURRENCE OF OCULOGYRIC CRISES IN IDENTICAL TWINS

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"Dartalan" is a phenothiazine derivative and is therefore related chemically to chlorpromazine. The manufacturers claim for dartalan qualitatively similar effects on the central nervous system of dogs to those of chlorpromazine. They further claim, however, that its tranquillizing and anti-emetic potency is approximately five to ten times greater by both oral and parenteral administration.

In discussing possible side-effects on human subjects the manufacturers state that signs suggesting involvement of the extrapyramidal system will appear in about one-third of *psychotic* patients receiving daily dosages of 80 mg. or more, that they have not been reported to occur in *non-psychotic* patients, and that they are rare even in *psychotic* patients who are receiving less than 50 mg. daily.

The present paper is concerned with our own findings only in so far as they concern the appearance of extrapyramidal signs in mentally defective patients who were given dartalan in an attempt to control their behaviour disorders.

The Investigation

Of the 31 patients 19 were female and 12 male. Their chronological ages ranged from 16 to 44 in the females and from 13 to 45 in the males and their I.Q.s from approximately 20 to approximately 70 in both females and males. In no case was there any history of a preceding encephalitis, nor were there any signs of extrapyramidal involvement before treatment.

One of the female patients suffered from major epilepsy and three from myoclonic epilepsy; three of the male patients suffered from major epilepsy.

Dosage.—Nineteen of the patients were given 10 mg. of dartalan t.d.s., five were given 10 mg. b.d., two were given 20 mg. b.d., four were given 20 mg. t.d.s., and one was given 30 mg. t.d.s.

Incidence of Parkinsonism.—Signs of Parkinsonism developed in 11 (57.9%) of the female patients and in four (33.3%) of the male patients. Their earliest appearance was on the fourth day in a male patient who was receiving 10 mg. of dartalan t.d.s. Six of the female patients who were receiving 10 mg. t.d.s., including a pair of identical twins, developed signs within seven days, one within 10 days on this dosage, one within eight days on a dosage of 20 mg. b.d., and one within nine days on a dosage of 20 mg. t.d.s.; one did not develop signs until the 25th day, and one not until the second month of treatment with 10 mg. t.d.s. In the other three male patients, signs appeared in one case on the sixth day on a dosage of 10 mg. t.d.s., in another during the fifth week on a dosage of 10 mg. b.d. throughout, and in the third on a dosage of 10 mg. t.d.s. for 14 days and 20 mg. t.d.s. for 19 days. The smallest total quantity of dartalan which produced signs of Parkinsonism was 100 mg., which a female patient had received in a dosage of 10 mg. b.d. for five days.

Of the female patients who did not develop signs of Parkinsonism one was receiving 10 mg. b.d., five (including a pair of identical twins suffering from myoclonic epilepsy) were receiving 10 mg. t.d.s., one was receiving 20 mg. t.d.s., and one 30 mg. t.d.s. The last was reported as showing excessive salivation one afternoon, but in the absence of any other conclusive signs of Parkinsonism she was not included in the affected group. Of the male patients who were unaffected, two were receiving 10 mg. b.d., one was receiving 20 mg. b.d., and five were receiving 10 mg. t.d.s.

None of the epileptic patients developed signs of Parkinsonism.

Development of Signs of Parkinsonism.—The earliest sign observed of the development of Parkinsonism was the loss of the associated movements of the arms, which were held semi-flexed at the elbow. Cog-wheel rigidity occurred early and was more marked in the arms than in the legs. Other early signs were the fixed mask-like or anxious facies and monotonous voice, the stooping attitude, and gliding steps. Tremor of the limbs appeared later as pronation and supination movements of the forearm, later developing into pill-rolling tremor of forefinger and thumb. Less frequently occurring signs were oculogyric crises (two females, two males), excessive salivation (one female, one male), and pseudo-catatonia (one female). One patient complained early in treatment of pain of a dull aching character in the shoulder girdle and upper limbs. Of particular interest was the development of oculogyric crises in a pair of identical twin female patients with a chronological age of 20 and I.Q.s below 25. Both were receiving 10 mg. of dartalan t.d.s. In one the oculogyric crises appeared on the fifth day of treatment and in the other on the sixth day.

E.E.G. Findings.—It was possible to arrange E.E.G. examinations while signs of Parkinsonism were present in only three cases (two female, one male). In each, low-amplitude slow components were recorded from all areas of the brain. In one of the female cases it was thought that the amplitude, distribution, and wave form of the slow components suggested the possibility of a deep-seated abnormality.

Reversal of Symptoms.—When conclusive signs of Parkinsonism appeared the same dosage of dartalan was continued and treatment with "disipal" (brand of orphenadrine) 50 mg. t.d.s. was started in all but one male who was given tab. bellad. ¼ gr. (16 mg.) b.d. In all but three cases the signs began to disappear within five days on this treatment, but in these three cases (two female, one male) it was necessary to increase the dose of disipal to 100 mg. t.d.s. before this occurred.

Discussion

In this small series of cases the incidence of Parkinsonism was much greater and occurred on a much lower and less prolonged dosage of dartalan than in any previously reported series. We consider it possibly significant, however, that, whereas all previous reports

have concerned patients of normal intelligence, all our patients were mentally defective. We suggest that in the genetically determined cases of mental defect, developmental abnormalities of and, in the environmentally determined cases, damage to the basal ganglia, insufficient in itself to produce signs of Parkinsonism, may considerably lower the threshold dosage of dartalan that can cause these signs to appear.

As we have stated, none of these patients had previously shown any signs of Parkinsonism, nor were any of them known to have suffered from encephalitis. It is well known, however, that a clear history of encephalitis in patients developing post-encephalitic Parkinsonism is frequently absent, and it seems probable that it would be absent in our cases if, as we suggest, the resulting damage was insufficient to produce post-encephalitic Parkinsonism of its own accord.

Summary

An account is given of the development of signs of Parkinsonism in 15 of 31 male and female mentally defective patients who were under treatment with dartalan, a phenothiazine derivative, in an attempt to control their behaviour disorders.

Attention is drawn to the occurrence of oculogyric crises in a pair of identical twins.

A possible explanation is suggested for the very much higher incidence of this complication of treatment with dartalan in this series than in any previously reported.

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INCIDENCE OF INTUSSUSCEPTION IN NEWCASTLE CHILDREN

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There are only two published estimates of the incidence of acute intussusception in this country. The first (Spence and Court, 1950) gave an estimated incidence of 3.8 per 1,000 live births in Newcastle upon Tyne in the years 1944 to 1949. The second (MacMahon, 1955) estimated that Birmingham children between 1945 and 1954 had an attack rate of only 1.49 per 1,000 live births. Both studies found evidence of variations in the attack rate from year to year.

It is a common impression that intussusception occurs more often in the North of England than in the Midlands and the South, and that it is more frequent in this country than in North America. The aetiology of intussusception is still unknown, but a difference of incidence as great as that described above is important enough for this impression to be tested and if possible brought to proof. For this reason it seemed worth while measuring the incidence in Newcastle again to see whether the previous high incidence, compared with Birmingham, was the result of two or three exceptional years or a persistent feature of the local scene.

Method

The method is identical with that used on other occasions (Davison, 1946; Spence and Court, 1950)—the enumeration of all children admitted to all Newcastle hospitals and giving a Newcastle address. The years chosen were 1950 to 1957. Reasons have been given in the papers referred to above why this can be regarded as a quantitative ascertainment for Newcastle. Only cases confirmed by operation (the majority) or by barium enema have been included, and suspected intussusceptions undergoing spontaneous reduction were not counted. When intussusception recurred, only the first illness was included.

This method of enumeration has the further advantage of being formally equivalent to MacMahon's. Like us, he counted all cases with a Birmingham address treated in any Birmingham hospital, included only cases where the diagnosis was confirmed, and excluded "instances of supposed spontaneous reduction without laparotomy."

Findings

In the eight years 1950 to 1957 there were 168 affected children and a steady rate of admission, none of the annual totals departing markedly from the yearly average of 21 (see Table). In the years 1950 to 1957 there were 39,100 live births to Newcastle residents. This may be taken as a sufficiently accurate denominator and gives an incidence of 4.3 per 1,000 live births.

Intussusception in Newcastle Children Between 1950 *and* 1957

	1950	1951	1952	1953	1954	1955	1956	1957	Total
Children affected	23	20	22	21	22	26	17	17	168

This figure confirms the previous findings in Newcastle and strengthens it, as the estimated incidence between 1944 and 1957—more than 4 per 1,000 live births—is based upon 295 cases (168 presented now, and 127 by Spence and Court, 1950). The estimate in Birmingham, 1.49 per 1,000 live births, was based upon 296 cases (MacMahon, 1955). With these figures there can be no doubt that the incidence in Newcastle is more than twice as high as that reported in Birmingham. This difference is the more remarkable because of the general similarity of the two cities in the occupations of the inhabitants, in the density of population, and in climatic conditions. Both the Newcastle and Birmingham studies depend, however, upon the supposition that not many children with intussusception and belonging to the two cities received treatment outside. Since the north-western border of Birmingham is an arbitrary rather than a natural boundary and merges with an extensive urban area containing a number of hospitals, is it possible that the observed difference could be an artifact?

There is some evidence tending to discount this possibility, derived from the measurement by the same method of the incidence of congenital pyloric stenosis in

the two cities. In Newcastle this was found to be 2.8 per 1,000 live births (Davison, 1946) and in Birmingham 3.0 per 1,000 live births (MacMahon, Record, and McKeown, 1951). The incidence of this disease has been measured on a number of occasions, and is relatively constant in different localities, and we may therefore conclude that the techniques of ascertainment in Newcastle and Birmingham are very similar in their degree of accuracy. Since pyloric stenosis and intussusception are alike in their hospital requirements it also seems safe to assume that the wide difference between the two cities in the incidence of the latter could not be due to a difference in the number of children treated in outside hospitals.

Conclusion

Clinical impressions and previous estimates of incidence suggested that acute intussusception was unusually common in the North of England. Because there have been so few factual studies the incidence of this disease has been estimated a second time in Newcastle and found to be persistently higher (over 4 per 1,000 live births) than in Birmingham (1.5 per 1,000 live births), the only other city for which it has been accurately assessed. The reasons for this difference are at present unknown, but the degree is sufficient to encourage the accurate measurement of incidence in other defined communities and to suggest the need for a more detailed analysis of local factors in the care of young children which might throw light on the aetiology of the disease.

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POLYAGGLUTINABILITY OF THE HUMAN RED BLOOD CELLS

BY

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The phenomenon in which the erythrocytes undergo transformation so as to become agglutinable by any serum, irrespective of the blood groups, can occur *in vitro* or *in vivo*, and presents a problem in correct grouping and matching.

The *in vitro* phenomenon is also known as the "Hübener–Thomsen–Friedenreich" phenomenon, and is seen usually in old blood samples with bacterial contamination. The very similar but more uncommon *in vivo* phenomenon has been termed "polyagglutination" to distinguish it from the *in vitro* phenomenon, termed "panagglutination," perhaps mainly on the ground of earlier observations that autoagglutination is not a feature of the former as it is of the latter. This has not been found to be true in all cases, and the consensus of opinion seems to be that the two phenomena are identical because of the outstanding fact that in most cases of polyagglutination a bacterial infection can be shown to be present. It is very likely that the enzymes liberated by the infecting organisms activate the "T" agglutinogen *in vivo* just as the enzymes of the contaminating bacteria do *in vitro*.

The subject has been discussed by Reepmaker (1952) and a good review of the recorded cases given.

Case Report

A blood sample from a patient suffering from septic abortion with profound toxaemia was received with an urgent request for blood transfusion. No history of previous conception or blood transfusion was given. The patient appeared to be group AB, Rh+ on repeated groupings by different batches of grouping sera, but one sample each of group AB, A, B, and O blood from stock was matched and only the group O was found compatible. Haemolysis of the incompatible cells by the patient's serum was pronounced. Her serum was tested against cell samples, five each from groups A, B, and AB and 10 from group O, freshly obtained from known donors (Table I). Her cells were tested against sera from these donors and two samples of cord blood serum (Table II).

Serum samples, one each from groups A, B, and AB, were adsorbed by equal volumes of three-times-washed packed cells of the patient, first at room temperature for one hour and then for another hour at 4° C., to adsorb the "T" agglutinin. The reactions of the adsorbed and unadsorbed samples are summarized in Table III. The patient's serum agglutinated at 4° C., group O cells also. Autoagglutination, though not detected at room temperature (near about 36° C. at this place during the season), was quite strong at 4° C. and could not be abolished even after prolonged adsorption at low temperature with group O cells.

TABLE I

	Group A Cells	Group B Cells	Group AB Cells		Group O Cells	
			Rh+	Rh−	Rh+	Rh−
Patient's serum:						
At room temp.	•••	•••	•••	•••	−	−
At 4° C. ..	++•	++•	++•	++•	++	++

+ = Agglutination. − = No agglutination. • = Haemolysis.

TABLE II

	Serum, Group A	Serum, Group B	Serum, Group AB		Serum, Group O		Serum, Cord Blood
			Rh+	Rh−	Rh+	Rh−	
Patient's Cells:							
At room temp.	++	++	++	++	++	++	−
At 4°C.	+++	+++	+++	+++	+++	+++	−

TABLE III

	Serum, Group A		Serum, Group B		Serum, Group AB	
	Ad-sorbed	Non-ad-sorbed	Ad-sorbed	Non-ad-sorbed	Ad-sorbed	Non-ad-sorbed
Patient's cells:						
At room temp.	−	++	−	++	−	++
At 4° C. ..	−	+++	−	+++	−	+++

Cultures were made from the patient's blood and the sample of pus collected from the cervical canal. Blood culture was positive within 24 hours. On bacteriological examination of the cervical swab and the patient's blood the same strain of *Escherichia coli* (typical type I) was isolated. Blood culture was negative a week later and the cervical sample was found unsuitable owing to frequent washings by antiseptic lotions.

Efforts to contact the patient for further investigations after her discharge from hospital have not been successful. Unfortunately, the culture materials, together with the organisms, were discarded after identification as a matter of routine before the scope of further investigations related to the problem could be realized.

Discussion

The reactions leave little doubt that the patient was group O, Rh+, presenting the phenomenon of polyagglutination, contamination being ruled out as the tests were made on fresh samples. Autoagglutination must have been partly due to the non-specific cold agglutinin, but mainly due to the "T" antigen–antibody reaction, as it persisted even after prolonged adsorption at low temperature with group O cells. It is not yet clear if any significance in relation to polyagglutinability can be attached to the presence of the specific haemolysins anti-A and anti-B, apparently in high titres.

Like most of the recorded cases, this case presented bacterial infection with features of septicaemia. In none of the reported cases, however, could the infecting organisms be isolated from blood culture (Reepmaker, 1952). That bacteriaemia could have been present in those cases also at some stage of the infection could not be ruled out, for blood culture is likely to be negative much before the organisms are eliminated from the local sites, and blood of a patient presenting polyagglutination will continue to show the phenomenon for some time after the control of the infection, until substantial numbers of the changed erythrocytes have been replaced by new ones.

What part bacteriaemia plays in the *in vivo* process can as yet be only a matter of conjecture However, it indicates, at least, bacterial growth severe enough to produce conditions approaching that *in vitro* for the enzymes to affect the erythrocytes. Presence or absence of associated bacteriaemia may perhaps be one of the explanations for polyagglutinability not appearing in bacterial infections with the regularity with which red cells undergo transformation *in vitro*. A direct proof has to be sought, and attempts must be made to test the ability of the organisms isolated from blood culture or local sites to produce the change *in vitro* as well. Meanwhile, there does not appear to be much objection to regarding bacteriaemia in the present case as strong evidence in favour of the common aetiology of the *in vitro* and *in vivo* phenomena.

Summary

A case of polyagglutinability of erythrocytes in a patient with septic abortion and severe *E. coli* infection and positive blood culture is described.

Its similarity to the Hübener – Thomsen – Friedenreich phenomenon is discussed, and that bacteriaemia in such cases could be strong evidence in favour of the common aetiology of the two phenomena is stressed.

I am indebted to Dr. B. P. Mishra, lecturer in bacteriology, Darbhanga Medical College, for the bacteriological report. It is hoped that with his collaboration more detailed investigations will be possible in future. Thanks are also due to Dr. Hari Prasad and Dr. M. Quadros, and Dr. S. M. Hashim, superintendent of the hospital, for permission to publish the case.

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Medical Memoranda

Aortography as an Aid to the Investigation of Haematuria

Generally, in the diagnosis of disease, radiology labours under the great disadvantage that a diagnosis can be made only when the disease has caused positive structural changes in an organ or in a system of organs. There is therefore a lapse of time between the onset of symptoms, which may sometimes be alarming, and the confirmation of the diagnosis by *x*-ray examination. The names of many diseases could be mentioned in which this time-lag occurs, the period showing a good deal of variation in time, largely depending on the severity of the disease; for example, bony metastases cause pain for some time before they become visible radiologically.

It is therefore necessary to use every available method of examination in the elucidation of symptoms in a difficult case. In the following case the patient was suffering from haematuria and the diagnosis was firmly established only by the use of percutaneous abdominal aortography.

VALUE OF AORTOGRAPHY

Most writers would argue that abdominal aortography is of considerable value in demonstrating the degree of obstruction in patients suffering from aortic and iliac atheroma, and also in showing the size and position of an aortic aneurysm.

Agreement concerning its value in the investigation of renal disease is not so unanimous. In the first place, conventional methods are often sufficient to establish the diagnosis, without resort to aortography. Secondly, if conventional methods show an abnormality the surgeon might well decide that he must operate on the kidney, in which case aortography (which is not without its risks) would seem to be unnecessary.

We have found renal aortography to be of value in a number of instances. (1) In proving the presence of a hypernephroma otherwise unsuspected. One of us (J. A. R.) was able to show a hypernephroma in the right half of a horseshoe kidney which was not shown by conventional methods. The case described below is a similar instance of its value. (2) It has been suggested that one type of unilateral disease with hypertension, suitable for treatment by nephrectomy, has the following features (Arthur Jacobs, 1958, personal communication): (*a*) non-function of one kidney on intravenous

pyelography, (*b*) the non-functioning kidney reveals a normal appearance on retrograde pyelography, (*c*) a block in the renal artery is demonstrated by aortography. Also Hodson (1957) suggested that an asymmetry of caliceal pattern may result from arterial lesions. Meaney *et al.* (1958) have shown that there is an absence of filling or diminution of interlobular arteries. (3) Aortography, by showing the pattern of the renal vessels, may be useful to the surgeon prior to performing a partial nephrectomy. (4) Aortography will confirm the presence of renal hypoplasia by demonstrating the poor arterial supply (Barr Stirling, 1957).

FIG. 1.—Aortogram taken on July 11. Swelling revealed below the ureteral pelvis.

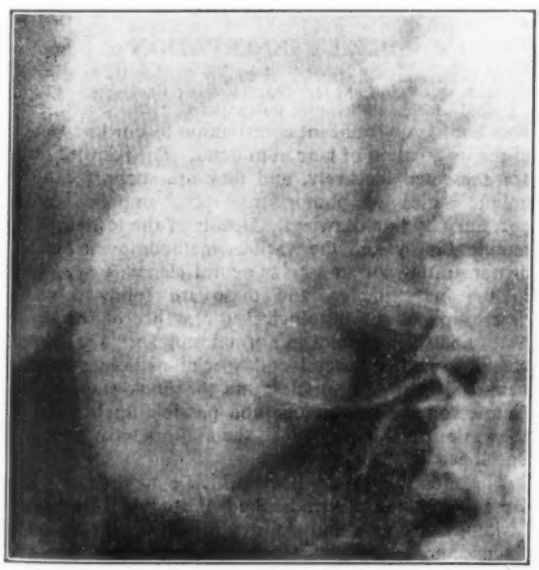

FIG. 2.—Aortogram taken on July 11, later phase. Nephrogram showing "blushing" in the renal substance.

A patient recently operated on by one of us (J. C. R.) was found to have only a rudimentary right kidney. The diagnosis was suggested by the aortogram, which showed complete absence of a right renal artery. There is therefore no doubt that renal aortography has an established place in diagnosis. Some claim that it is possible to distinguish between renal cyst and hypernephroma by means of aortography. This is often true, but there is always the doubtful case, so that abdominal aortography cannot always be the final arbiter in the distinction between cyst and tumour.

CASE REPORT

The patient, a man aged 36, was admitted to hospital on June 2, 1958, complaining of haematuria and of severe pain in the right loin, radiating to the groin. Suprapubic pain and relative frequency were also present. On examination there was marked tenderness in the right loin and flank. Cystoscopy revealed a blood-stained efflux from the right ureter, but a right retrograde pyelogram was normal. An intravenous pyelogram also showed normal appearances, so it was thought that the haematuria was possibly due to a small papilloma in the renal pelvis. He was discharged pending more definite evidence pointing to the necessity of exploring the right kidney. On October 3 he was again admitted with the same symptoms of pain and haematuria, which were not so severe on this occasion. Once again intravenous pyelography and a right retrograde pyelogram revealed a normal appearance. Aortography was performed because the previous conventional methods had not yielded any information. The films (Figs. 1 and 2) showed that there was a small oval swelling of the kidney, below the pelvis, and at a later phase that there was some "blushing" in the renal substance. A diagnosis of hypernephroma was suggested.

FIG. 3. — Specimen removed at operation.

A relatively small hypernephroma was found at the site of the swelling, extending into the kidney. Fig. 3 shows the photograph of the kidney, removed at operation.

CONCLUSION

We believe that, when elderly patients are suffering from haematuria for which an explanation cannot be found by conventional methods of *x*-ray examination, abdominal aortography should be considered.

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Reviews

AUTOBIOGRAPHY OF A NEUROSURGEON

Fifty Years of Neurosurgery: A Personal Story. By Ernest Sachs, M.D. (Pp. 186; illustrated. $3.50.) New York: Vintage Press. 1958.

This book, which had scarcely appeared before its author died in his 80th year, begins with an interesting sketch of the life of a New York schoolboy, the son of the head of one of the leading private schools of that city. Sachs was brought up strictly in a Victorian sort of way, reminding the reader of the semi-patrician society of Henry James's *Washington Square*, for this was in the 1880s and 1890s, and horse cars ran in New York's streets. Hans Zinsser and Herbert Lehman, later Governor of New York, were school-fellows. No less interesting is Sachs's description of his life at Harvard, and, his tastes having been turned to medicine as well as to music by his uncle, the famous neurologist Bernard Sachs, he entered the Johns Hopkins Medical School in 1900 when it was at the peak of its fame. Franklin Mall, William Howell, with Joseph Erlanger as assistant, were there as well as the Great Four. Young Harvey Cushing came as resident, and then was instructor in surgery during Ernest Sachs's studentship. After graduation, and having now, prodded by his uncle, decided to try whether he could improve the then far from encouraging results of brain surgery, he went, after six months in Oppenheim's clinic in Berlin, to work for over a year with Sir Victor Horsley. He quickly became Horsley's devoted admirer, and remained one until his death, as did many others. Sachs's chapter on Horsley is important historically. All his life he was a welcome visitor in Britain, and was a notable friend of this country.

When Sachs was coming home in 1908 Cushing offered him a post in Baltimore, but Sachs declined, as he wished to finish his London research. He was eventually appointed to the Beth Israel Hospital in New York, and later to the Bellevue, until in 1911 he moved by invitation to St. Louis, where his destiny lay during the next 30-odd years. There his great work was done, a lone but vital outpost of neurosurgery far from, but linked with, the thriving neurology and neurosurgery of the Atlantic seaboard. The rest of this autobiography describes his work and that of the eventually distinguished pupils who worked with him. Sachs, who was a devoted family man, tells at length of their travels in Europe and South America, and again of vacation life in his beloved Adirondacks with his inseparable charming and talented companion, Mrs. Maisie Sachs.

Ernest Sachs was one of the most important figures in the development of modern neurological surgery. He was distinguished by an immense vitality, a huge appetite for work, by his honesty, modesty, and frankness. He had wide interests in medical education and in the training of the surgeon. His several books bear witness to this, as do the 170-odd papers that came from his own pen or from those of his pupils. The quality of Sachs's contributions at the time that they were made marks him as one of that small band who, by the exceptional standards they set, their scientific drive, and their unselfish devotion, made neurosurgery what it is to-day.

GEOFFREY JEFFERSON.

FUNGOUS DISEASES

Fungous Diseases and their Treatment. Edited by R. W. Riddell, M.D.(Lond.), F.R.C.P.(Edin.), and G. T. Stewart, B.Sc., M.D.(Glas.), D.T.M.&H. (Pp. 254+xvii+8; illustrated. 45s.) London: Butterworth and Co. (Publishers) Ltd. 1958.

After the fundamental work of Sabouraud, Whitfield, Adamson, and others early in the century, there had until recent years been little progress in our knowledge of the fungi responsible for disease in the human. The increased incidence and varied presentations of such disease in temperate climates have stimulated research again, and at a conference in London in 1957 much of this work was brought together and presented to the profession. This volume is a record of the papers presented and is of value to dermatologist and physician.

The subject is introduced by Riddell with clarity and proportion, and this is followed by chapters on histopathology and pathogenesis. Vanbreuseghem, from a wide experience, discusses the role of the soil in regard to the life history of fungi and stresses the importance of deficiency states in predisposing the human to parasitic invasion. There is a chapter by Calnan on the varied clinical features of *Trichophyton rubrum* infections, which steadily increase and are difficult to treat. Much work on candidiasis is presented. The association with steroid and antibiotic therapy, with endocrine, renal, and pancreatic disease, is discussed and treatment is effectively reviewed. There are papers on pigment formation and immunity, and on the more recent development in fungicidal antibiotics. The work is not limited to superficial dermatophytes, but includes the deeper and systemic infections, uncommon in Great Britain, as actinomycosis, mycetoma, and histoplasmosis. There are important contributions on the pulmonary mycoses and their treatment.

This is a stimulating and promising record of the renewed interest in the mycoses. Advances are likely to be rapid, and the recent introduction of griseofulvin for some incurable infections is a further herald of progress.

J. T. INGRAM.

MUSCLE INNERVATION

The Innervation of Muscle. A Biopsy Study. By C. Coërs and A. L. Woolf, M.D. (Pp. 149+xv; illustrated. 42s.) Oxford: Blackwell Scientific Publications. 1959.

This book is a significant contribution to our knowledge of the innervation of human muscles. The relevant facts are presented incisively, and they are supported by a unique series of photomicrographs, amplified when necessary by line drawings. Details of the technique of muscle biopsy and the various methods available for demonstrating intramuscular neural elements are given in the first chapter, and these are followed by a description of the histological appearance of the nerve fibres and their endings in normal muscles. Then come chapters on the general and special pathology of the neural elements in muscles, and the book ends with a chapter on the significance and possible application of the various techniques which the authors have used and developed in their studies.

The most important point which emerges from this work is that the proper method of studying the neurohistology of human muscle is by means of biopsies from living human beings; it cannot be inferred from the study of animal muscles. For example, in man nerve endings closely resembling the flower-spray endings of the cat muscle cannot be found. The reason for this is

not clear, but it may be due to the greater length of the spindles in man and the correspondingly greater dispersion of the various motor endings. The studies reported in this book also confirm and re-emphasize the fact that both motor and sensory peripheral nerves are living structures and thus have a labile morphology. This, together with the complex patterned arrangement of peripheral nerve fibres in the tissues which they supply, makes it clear that models designed to illustrate their functional activity must be based on the notion of probability and discussed in statistical language.

The task which the authors set out to accomplish was formidable. Yet, in spite of the facts that one of them lives in Belgium and the other in England, and that the specimens were collected from numerous centres in Belgium, France, and England, it has been accomplished, and in a most elegant and impressive manner.

G. WEDDELL.

SOFT-TISSUE TUMOURS

Tumors of the Soft Somatic Tissues. By George T. Pack, M.D.; LL.D., F.A.C.S., and Irving M. Ariel, M.D., F.A.C.S. (Pp. 820+xvi; illustrated. £11 11s.) London: Cassell and Co., Ltd. 1958.

The title of this book is mildly intriguing and conjures up thoughts of a fascinating companion volume on "Tumors of the Hard Psychic Tissues." Wayward thoughts being put aside, we find a clinical treatise dealing with tumours of soft tissues. It considers tumours, and tumour-like proliferations, of fibrous tissue, primitive mesenchyme, fat, blood and lymph vessels, synovial tissue, muscle, and the peripheral nervous system. Tumours arising in parenchymal organs are excluded, as also are tumours of the lympho-reticular system. Included are some rather strange bedfellows such as carcinoma-sarcoma of the uterus and nephroblastoma of the kidney—the latter masquerading under the archaic title of embryonal adenomyosarcoma. The authors are surgeons. They are assisted by 15 collaborating authors, surgeons all apart from a dermatologist and a pathologist, who hail mainly from the United States, but include one representative each from Brazil, Canada, and Paraguay. Much of the book is based on the experience of this group, over a period of 25 years, at the Memorial Center for Cancer and the Pack Medical Group in New York. A measure of this experience is an analysis of 717 malignant soft-tissue tumours.

The book is divided into six sections. The first deals with the classification and natural history of various tumours. The next section considers the general principles of treatment; it includes a detailed account of amputations, and has chapters on biopsy technique and radiation therapy. Section III forms two-thirds of the book, and considers the pathology, clinical features, and treatment of individual tumours. Short sections follow on "Tumors in Infants and Children" and on "Regional Anatomic Considerations." The last section, on "Prognosis," consists of a brief series of tables and charts showing the end-results of treatment. The volume is well produced and lavishly illustrated, but very expensive. Some of the photomicrographs are poor, and few state the magnification. Tables 5 and 67 are identical, so are Figs. 293 and 440, although their respective case reports, Nos. 50 and 80, are sufficiently dissimilar to cause difficulty in identification. The text is a little discursive, but the book contains much information and should be a useful work of reference for surgeons and pathologists.

B. S. CARDELL.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

Pathology. By Peter A. Herbut, M.D. Second edition. (Pp. 1,516; illustrated. £6 18s.) London: Henry Kimpton. 1959.

Dermatologie und Venerologie. Edited by Professor Dr. H. A. Gottron and Professor Dr. W. Schönfeld. Volume III, Part I.

Moloy's Evaluation of the Pelvis in Obstetrics. By Charles M. Steer, M.D., Med.Sc.D., F.A.C.S., F.A.C.O.G. Second edition. (Pp. 131+ix; illustrated 28s.) Philadelphia, London: W. B. Saunders Company. 1959.

Physiology of Motion. Demonstrated by Means of Electrical Stimulation and Clinical Observation and Applied to the Study of Paralysis and Deformities. By Dr. G. B. Duchenne (of Boulogne). Translated and edited by Emanuel B. Kaplan, M.D. (Pp. 612+xxiii; illustrated. 77s.) Philadelphia, London: W. B. Saunders Company. 1959.

The Gifted Group at Mid-Life. Thirty-five Years' Follow-up of the Superior Child. By Lewis M. Terman, and Melita H. Oden. (Pp. 155+xiii; illustrated. 36s.) Stanford, California: Stanford University Press. London: Oxford University Press. 1959.

Current Drug Handbook. By Mary W. Falconer, R.N., M.A., and H. Robert Patterson, B.S., M.S., Pharm.D. 1959-1960. (Pp. 161+viii. 19s.) Philadelphia, London: W. B. Saunders Company. 1959.

Radiation Therapy. By Walter T. Murphy, M.D. (Pp. 1,041+xiii; illustrated. £8 15s.) Philadelphia, London: W. B. Saunders Company. 1959.

Medical X-Ray Technique, Principles and Applications. By G. J. Van der Plaats. (Pp. 480+xii; illustrated. 57s. 6d.) Eindhoven: Philips' Technical Library. London: Cleaver-Hume Press Ltd. 1959.

An Atlas of Normal Radiographic Anatomy. Second edition By Isadore Meschan, M.A., M.D. With the assistance of R. M. F. Farrer-Meschan, M.B., B.S. (Melbourne, Australia), M.D. (Pp. 759+xii; illustrated. £5 12s.) Philadelphia, London: W. B. Saunders Company. 1959.

Pharmacology of Some Toxins. By Professor Helena Rašková, M.D. (Pp. 132; illustrated. 28s.) Prague: Publishing House of the Czechoslovak Academy of Sciences. London: Collett's Holdings Ltd. (Bookshops). 1958.

Le Sindromi Neuropsichiche da Carenza Alimentare. By Giuseppe Pintus, Alberto Muratorio, and Aldo Giannini. (Pp. 289. L. 3,000.) Pisa: Edizioni "Omnia Medica." 1959.

A Mount Sinai Hospital Monograph on Systemic Lupus Erythematosus. Editors: George Baehr, M.D., and Paul Klemperer, M.D. (Pp. 84+iv; illustrated. $3.75.) New York, London: Grune and Stratton. 1959.

L'Expertise de la Silicose Pulmonaire. By Paul Sadoul and Maurice Dusapin. (Pp. 234; illustrated.) Paris: Masson et Cie, 1959.

Pigment Cell Biology. Proceedings of the Fourth Conference on the Biology of Normal and Atypical Pigment Cell Growth. Edited by Myron Gordon. (Pp. 647+xiv; illustrated. $13.50.) New York: Academic Press Inc., Publishers. 1959.

Reproduction in Domestic Animals. Edited by H. H. Cole and P. T. Cupps. (Pp. 651+xv; illustrated. $14.50.) New York, London: Academic Press. 1959.

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VACCINATION AGAINST TUBERCULOSIS

Views on the value of vaccination with B.C.G. vary widely from country to country. In Scandinavia, as in many other European countries, its efficacy has long been accepted on the basis of evidence which, although often highly suggestive, was not completely conclusive. As a result of this enthusiasm many millions of people in under-developed countries were vaccinated under the auspices of the international B.C.G. campaign. In this campaign the value of the vaccine was regarded as established and few steps were taken to confirm its usefulness in the field. In the United States the attitude has been much more critical. One group, whose views were summarized in a recent article[1] in this *Journal*, sweepingly condemn B.C.G. mainly because its widespread use would lead to the loss of tuberculin-testing as a case-finding and epidemiological weapon. The title of their paper, "The Case Against B.C.G.," confessed a prejudice which many readers found well borne out in the text. Another group in the United States base their objections mainly on the relatively meagre value of vaccination shown in the preliminary reports of the trials carried out by the United States Public Health Service.[2]

It is not surprising that there should be these differences of opinion. Not only have there been great variations in the design of trials but there may also be differences in the quality and quantity of the vaccine and in the epidemiological situation in which it is used. The object of vaccination with B.C.G. is to give the individual a harmless primary infection with avirulent tubercle bacilli which will confer immunity against a later virulent infection. To take two extremes, B.C.G. would clearly have little effect on the incidence of tuberculosis in a population mostly composed of people who had already been infected with virulent tubercle bacilli, or, on the other hand, in a community which was experiencing no natural infection at all. It is possible that the effect will be greater, or at least immunity may last longer, if those vaccinated are subsequently subjected to small natural superinfections of virulent bacilli which previous vaccination enables them to overcome. It may be that in certain parts of the world there are natural infections with some unknown organisms which confer on the individual a low degree of sensitivity to tuberculin and possibly also some degree of immunity to virulent tubercle bacilli.[3] This might offer a partial explanation for the considerable differences in the efficacy of B.C.G. found in the trials conducted by the United States Public Health Service and by the Medical Research Council in Britain.

The first report[4] by the Tuberculosis Vaccines Clinical Trials Committee of the Medical Research Council was published in this *Journal* early in 1956, and the second appears in our opening pages this week. The report concerns the trial both of B.C.G. and of vole-bacillus vaccine, although the former is of more immediate practical interest. Some 56,700 schoolchildren in urban or suburban areas in England took part in the trial: they had volunteered, with their parents' consent, for vaccination between September, 1950, and December, 1952. All were aged between 14 and 15½ years. The children were initially tuberculin-tested and had a radiograph of the chest taken. Those found to have active tuberculosis were excluded from the trial. Those with normal radiographs but a positive tuberculin-test were followed up in the same way as those in the vaccinated and control groups. The children who proved to be tuberculin-negative were divided at random into vaccinated and unvaccinated groups.

The task of follow-up has been a formidable one, but remarkably successful. A sample analysis has shown that some 90% of the participants were contacted by one means or another during the two years 1957 and 1958. Subsequent cases of tuberculosis were identified either through the National Health Service, by postal contact with the participants, or by radiographs of the chest taken by the teams responsible for the follow-up. When any participant was found to have developed a disease which might possibly be tuberculosis, the details, with the exception of data about tuberculin-testing and B.C.G. vaccination, were submitted to an independent assessor unaware whether or not the patient had been vaccinated. The assessor decided whether the case should be regarded as one of tuberculosis. Great efforts were made to avoid prejudice, and it seems virtually certain that these were successful.

The second report presents results for all participants who have been in the trial for five years, with preliminary incomplete information up to seven-and-a-half years. During the five-year period the annual

[1] Anderson, A. S., *et al.*, *Brit. med. J.*, 1959, **1**, 1423.
[2] Palmer, C. E., *et al.*, *Amer. Rev. Tuberc.*, 1958, **77**, 877.
[3] Palmer, C. E., *Bull. int. Un. Tuberc.*, 1957, **27**, 106.
[4] *Brit. med. J.*, 1956, **1**, 413.

incidence of tuberculosis in the B.C.G.-vaccinated group was 0.38 per 1,000 participants, compared with 2.29 per 1,000 among those in the tuberculin-negative unvaccinated group. The reduction in tuberculosis attributable to vaccination is thus 83%. The incomplete information up to seven-and-a-half years shows that a similar high degree of protection has continued. Of the cases of tuberculosis that arose in both the vaccinated and unvaccinated group, some 70% were pulmonary disease. The protection against tuberculous pleural effusion and enlargement of the hilar glands was similar to that afforded against pulmonary tuberculosis. On the other hand, the small number of cases of miliary tuberculosis and tuberculous meningitis all occurred among unvaccinated individuals. Among the vaccinated group not only were there very many fewer cases of pulmonary tuberculosis but there was also some evidence that those which did occur were rather less severe.

The vaccine used in the trial was the Danish liquid vaccine which until recently has been in routine use in the United Kingdom. As usual, the viable count varied slightly from batch to batch, but even the batches with the lowest counts gave substantial protection.

The protection afforded by vole-bacillus vaccination was at least as good as that by B.C.G. The strength of the early batches of vole-bacillus vaccine was below the standard intended, and the tuberculin conversion rate was notably less than with the later batches, which had been brought up to strength, or than with B.C.G. Nevertheless, these earlier weaker batches conferred substantial protection against tuberculosis and were not associated with lupus vulgaris at the site of vaccination, sometimes a troublesome complication of the stronger vaccine. At the present time, however, there is little suggestion of any positive advantage from the use of the vole vaccine.

Both the design and the execution of this trial reflect great credit on all those concerned. It has been shown conclusively that Danish liquid vaccine given to schoolchildren aged 14–15½ in urban Britain confers substantial protection against tuberculosis, and that this protection lasts for at least five years and probably for six years or more. As a notable amount of tuberculosis occurred among children with positive tuberculin tests but with no radiographic evidence of infection at the beginning of the trial, the question arises whether the vaccine should not be given at an earlier age, when fewer children have been naturally infected. Since the beginning of the trial epidemiological circumstances have changed substantially, and the proportion of tuberculin-positive schoolchildren is falling rapidly in most areas. Although it might perhaps be justifiable to move back the age of vaccination to, say, 10 years, the effect of this on the still-undetermined question of the duration of immunity would have to be considered. If the immunity conferred by B.C.G. began to wane after, say, seven years, then the adolescent might be left relatively unprotected during the susceptible ages of 17 to 25. In most of the schemes arranged by local authorities children are now vaccinated between the age of 13 and 14 years, and perhaps the arguments are not at present strong enough to alter this routine.

As yet a relatively small proportion of the population of the United Kingdom is protected by B.C.G. Although this proportion is increasing, it will probably be a number of years before vaccination with B.C.G. makes a really substantial contribution to the reduction of tuberculosis in the population as a whole. Under the conditions in which it has been used in Britain B.C.G. is highly effective, but it is only one of the many weapons which must be used in the eradication of the disease.

CONTROL OF PLAGUE

In past centuries the ravages of epidemic plague made it possibly the most devastating of the pestilential diseases. In recent years, however, international transmission appears to have ceased,[1] and it is worth considering to what extent the disease remains a menace to world health. The epidemiology, therapy, and control of plague have recently been reviewed by an expert committee of the World Health Organization, whose report[2] has confirmed that this infection is still endemic among animals in various parts of the world—in northern China, south-western United States of America, foci in the eastern, western, and central parts of South America, the northern provinces of India, Java, Central Asia, Madagascar, the Soviet Union, Iranian Kurdistan, the Union of South Africa, the Belgian Congo, and a recently described focus in Kenya. In these sylvatic foci plague persists in wild rodents possessing some degree of resistance to the infection, and these form a permanent reservoir from which the disease may spread as an epidemic through "semi-domestic" rodents to rats and mice and thus to man. Transmission may also spread to rats and man in other, and even distant, localities by the carriage of infected rats and their fleas. So long as these permanent sources of plague exist there will continue to be a local risk of transmission sporadically to man,

[1] *Chron. Wld Hlth Org.*, 1956, **10**, 292.
[2] *Wld Hlth Org. Tech. Rep. Ser.*, 1959, No. 165.
[3] Brygoo, *et al.*, *Arch. Inst. Pasteur Tananarive*, 1957, **26**, 124.

but the danger of more distant spread is steadily diminishing owing to the wider adoption of measures against "domestic" rodents (rats and mice) and the efficiency of techniques for the control of plague. Elimination of an endemic focus among wild rodents has only recently been attempted, and it has proved expensive and difficult.

Measures for the control of plague may be directed towards the wild rodent reservoir, the domestic rodent, or to man in contact with these animals. Populations of domestic rats may be reduced by the use of poison baits or by gassing their burrows with chloropicrin or cyanide, and these methods have also been used successfully by Russian workers in an attack on the wild rodents in sylvatic foci of plague. The most rapidly effective control measure in epizootics or epidemics remains the destruction of vector fleas by means of insecticides applied to all surfaces over which rats may move. The susceptibility of man to infection can be reduced by vaccination, but the vaccines are not highly efficient, and in present circumstances this method of prophylaxis is best used to raise immunity progressively (by giving the vaccine annually) among communities in the neighbourhood of enzootic foci.

Treatment of plague improved greatly with the introduction of the sulphonamides and antibiotics. Sulphamerazine is the most popular drug, but it is ineffective in pneumonic plague unless given very early. In this form of the infection streptomycin proved very effective both in treatment and prophylactically in contacts,[2] but recently it has been reported that it is apt to produce a high degree of resistance in *Pasteurella pestis*. The tetracycline group of antibiotics have proved to be as active as streptomycin and more useful because they can be given by mouth and are less toxic.

So long as enzootic foci persist in wild rodent populations plague remains a threat to human communities in contact with them. Owing to the effectiveness of control measures against domestic rodents international spread is now limited, and the use of preventive techniques to eliminate foci of wild rodent plague, successfully introduced by the Soviet Union,[2] gives the hope that the world will be rid of this pestilential disease in the foreseeable future.

ROYAL COLLEGE OF PHYSICIANS

The Isaac Wolfson Foundation has made the princely grant of £450,000 to the Royal College of Physicians of London for the building of its new premises. (An account of the Foundation appears on p. 427.) Earlier this year[1] the College announced that it is surrendering the lease of its building and site in Pall Mall to the Government of Canada. It is to become part of Canada House. The present College was built by Sir Robert Smirke and was opened in 1825 by Sir Henry Halford, P.R.C.P. There were then only 90 Fellows. For some time now the College has felt the discomforts of its restricted accommodation. There are now some 900 Fellows and 4,000 Members. But quite apart from this increase in numbers this ancient institution needs room to expand if it is to live up to its responsibilities in the modern setting of twentieth-century medicine. Sir Robert Platt, P.R.C.P., and his fellow officers have been fortunate to acquire a site at the south-east corner of Regent's Park, and the great generosity of the Isaac Wolfson Foundation, together with the money from the sale of its present house, will enable the College to set about planning a new house in the full confidence that it will be able to complete it so as to make a new habitation fit for its ancient name. The Royal College of Physicians of London is a national possession with an international reputation, and so the whole of the profession will want to join with the College in expressing deep gratitude to the Isaac Wolfson Foundation and to Mr. Wolfson.

[1] *Brit. med. J.*, 1959, 1, 852.

STEROID THERAPY IN MUMPS

Orchitis is the most common and most troublesome complication of mumps. An incidence of 25% in adult males is generally accepted,[1] though a figure as high as 67% has been reported. Meningitis or meningo-encephalitis is also not uncommon. In one outbreak[2] the incidence was 6.3%. Other workers[1] reported an incidence of 54%, but they based their figures on studies of the electroencephalogram and cerebrospinal fluid rather than on clinical findings. Pancreatitis and oophoritis, facial and trigeminal neuralgia, iritis, and deafness are all well-known, though rare, complications. Myocarditis has been reported[1] in 4.4% of cases, hepatitis has been suspected,[3] and recently[4] thrombopenic purpura has been described in three patients. Before steroid therapy became available, very little, other than an operation for orchitis, could be done to cure or relieve any of these conditions. The claims for steroid therapy are therefore worth considering.

G. C. Risman[5] reported the use of cortisone in five patients suffering from orchitis. He gave 300 mg. on the first day, followed by at least 100 mg. daily for several days. The results were not dramatic, but pain and tenderness were relieved in 24 hours. Three of the five patients while still taking the drug developed orchitis in the other tes is: it was milder and of shorter duration. I. M. Smith and J. W. Bishir[6] gave 300 mg. cortisone daily for three to four days; this appeared to relieve the pain but had less certain effect on the swelling and temperature, and did not prevent the onset of orchitis or its spread to the other testis. R. G.

Petersdorf and I. L. Bennett[7] treated 23 patients; they gave 300 mg. cortisone on the first day of treatment, followed by 200 mg. daily for 3 to 18 days, the average course being 1,100 mg. given over seven days. In 22 of the patients pain and tenderness were strikingly relieved within 24 hours; the mean duration of temperature was 36 hours. The authors attempted to study the effect on subsequent atrophy of the testis, and of 13 patients they found evidence of atrophy in five, three of whom had taken longer than the average to respond to the treatment. It is impossible to estimate the value of this finding, because the frequency of testicular atrophy in the untreated case is not known. The incidence of sterility has possibly been overestimated, and most physicians of experience will know of instances where sterility has not resulted even after severe bilateral orchitis. But it seems clear that cortisone, or a similar adrenal steroid, given in a dose corresponding to 300 mg. of cortisone daily for several days, does usually produce rapid relief from pain and tenderness. It seems clear that the drug may not prevent the occurrence of orchitis in the unaffected testis, so that it would be wrong, and perhaps dangerous, to give it prophylactically to patients with parotitis. The only other treatment known to give relief in mumps orchitis is incision of the tunica albuginea under anaesthesia. Steroid therapy seems to produce comparable results, though it requires further study.

The use of steroids in meningo-encephalitis is more difficult to assess. This complication, though it may be very severe, usually clears up completely without specific therapy. J. K. Spitznagel[8] treated four patients with 50–75 mg. cortisone every six hours, and one patient with 15 mg. adrenocorticotrophic hormone (A.C.T.H.) every six hours for 6 to 17 days. The drugs appeared to produce rapid remission of symptoms, and abrupt withdrawal caused a rapid recurrence of all symptoms in one patient. This would appear to suggest that the drug can influence the course of this complication, though whether its use is justified is another matter. A similar trial[9] was reported in ten patients with measles encephalitis, and here again while the drug did appear in some cases to produce clearing of the sensorium it was doubtful whether in such a variable disease it really affected the prognosis. W. W. Spink[10 11] stresses that, while the judicious and prompt use of the adrenal steroids will sometimes prevent fatalities, they should not be given unless backed by a reasonable assurance that they will alter the illness favourably.

Thrombopenic purpura has been reported[12] as a complication of mumps, though it is doubtful whether it is a true complication rather than a pre-existing condition triggered off by the infection. Three patients developed severe purpura and bleeding after the onset of mumps, and in these cases steroid therapy appeared to control the bleeding, though in two the deficiency of platelets was not corrected until after splenectomy. While mumps is worth bearing in mind as a possible cause of purpura, it is in the other two complications of mumps, orchitis and meningoencephalitis, that the role of steroid therapy needs to be more clearly defined. At present it appears to be of rather doubtful effect in meningoencephalitis but well worth trying in orchitis.

1 Bengtsson, E., and Örndahl, G., *Acta med. scand.*, 1954, **149**, 381.
2 Russell, R. R., and Donald, J. C., *Brit. med. J.*, 1958, **2**, 27.
3 Warren, W. R., *Arch. intern. Med.*, 1956, **98**, 525.
4 Kolars, C. P., and Spink, W. W., *J. Amer. med. Ass.*, 1958, **168**, 2213.
5 Risman, G. C., ibid., 1956, **162**, 875.
6 Smith, I. M., and Bishir, J. W. *New Engl. J. Med.*, 1958, **258**, 120.
7 Petersdorf, R. G., and Bennett, I. L., *Arch. intern. Med.*, 1957, **99**, 222.
8 Spitznagel, J. K., *Ann. intern. Med.*, 1958, **49**, 61.
9 Ilen, J. E., *Pediatrics*, 1957, **20**, 87.
10 Spink, W. W., *New Engl. J. Med.*, 1957, **257**, 979.
11 —— ibid., 1957, **257**, 1031.
12 Kolars, C. P., and Spink, W. W., *J. Amer. med. Ass.*, 1958, **168**, 2213.

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INSECT STINGS

Most people take simple common-sense measures after being stung by an insect and do not consult their doctor unless severe reactions occur. Identification of the insect is of academic importance only, for the treatment of stings is not very specific, and in any event the badly stung victim is usually sore and angry and his main concern is to escape. Even so, a quick look may show a bee-sting *in situ*. The honeybee is peculiar in that she leaves her sting and poison apparatus behind, and these go on injecting venom for several seconds.[1] Hence advice that the sting should be "gently removed" is bad, for this would squeeze the poison sac. The bee-sting should be scraped out with the finger-nail or wiped out with a handkerchief. Antihistamine creams *promptly* applied are of some help. Stings on the back of the neck have a bad reputation, possibly because of reflex vagal stimulation.

The severe generalized reaction calls for medical help and probably occurs more commonly than is generally supposed. The usual treatment is to give 0.5 to 1.0 ml. of adrenaline injection *B.P.* (1 in 1,000) subcutaneously (an ampoule-syringe ensures prompt administration), followed by 50 mg. of cortisone acetate intramuscularly and an antihistamine tablet by mouth.

Prophylaxis for patients who are known to react badly presents a difficult problem. Many workers[2 3] have shown that the antigen causing the reaction is present throughout the whole insect and not simply in the venom. The recently described queen substance of honeybees,[4] for example, is known to be distributed widely among worker bees, but its allergic possibilities remain uninvestigated. M. Schacter and E. M. Thain[5] have shown that the most important substance in wasp venom is a polypeptide called kinin. Although sensitivity may occur to these special substances in different insects it is not always species specific, and thus mixed extracts of whole insects are usually given for desensitization. Testing with solutions as weak as 1 in 10 million shows that extreme sensitivity may occur in some patients.

In a study of 84 patients who suffered systemic reactions to bee- and wasp-stings, H. L. Mueller[6] found that 75% gave a personal or family history of allergy.

1 Birch, C. A., *Med. Press*, 1956, **235**, 479.
2 Perlman, E., *J. Mt Sinai Hosp.*, 1955, **22**, 336.
3 Rockwell, E. M., *Ann. Allergy*, 1952, **10**, 404.
4 Butler, C. G., *The World of the Honeybee*, 1954, London, chapter 8.
5 Schacter, M., and Thain, E. M., *Brit. J. Pharmacol.*, 1954, **9**, 352.
6 Mueller, H. L., *New Engl. J. Med.*, 1959, **261**, 374.

The more rapid the onset of symptoms the more severe the reaction was likely to be. Desensitization may be thought to be advisable from the history alone, and then should be started by a small dose of a weak dilution of whole-body extract of one kind or several kinds of insects. The initial dose depends on the severity of the patient's reaction to stings and may vary from 0.05 ml. of a 1 in 10 million dilution to 0.05 ml. of a 1 in 10,000 dilution. The dose should be increased gradually until a dose of 0.2 to 0.3 ml. of a 1 in 100 dilution is tolerated. Alternatively, intracutaneous tests may be used to find out the weakest dilution which causes a skin reaction, and immunization should then be started with a dose of this strength. A few patients who have suffered severe allergic reactions to bee-stings do not show sensitivity to skin tests. Adrenaline should always be available when giving these injections.

Mueller recommends that all patients should receive a maintenance dose of antigen every four weeks during the insect season and every six weeks throughout the winter for three years. Further study may decide whether less frequent booster doses (say four a year) are effective. Mueller's results show that with one exception all patients stung while on a maintenance dose of 0.15 ml. or more of a 1 in 100 dilution of mixed extract, or who were stung after receiving treatment for three years, did not have systemic reactions.

STEELY EYES AND PAIN

Differences between patients in their response to pain are apt to set the medical man many a diagnostic puzzle in the course of his professional life. What one person has dismissed as a mere flea-bite another will declare was an excruciating stab. Moreover, "despite all verbal shortcomings and exaggerations there exists an obvious difference in the pain reaction of individuals to what is, as near as possible, an identical stimulus."[1] As Macdonald Critchley, the author of these words, goes on to point out, "common experience teaches that the burly, lymphatic artisan feels pain less than the fragile artist or thinker." Though a generalization of that kind stimulates the reader to think of the exceptions to it that he can probably recall, there is doubtless some connexion on the average between reaction to pain and, among other factors, body build, occupation, nationality, education, and health.

Now a surprising association has been noted—namely between reaction to pain and colour of eye. P. R. N. Sutton,[2] of Melbourne University Dental School, studied 403 consecutive subjects whose teeth were being prepared for filling by a high-speed drill. They were Australians of European stock, and their ages ranged from 3 years to more than 50. He classified the reactions to pain in four categories and colour of the iris in nine. The judgments were admittedly subjective, but classifying some of the patients again showed that the judgments were reproduced fairly closely. On comparing colour of iris and reaction to pain, he found that the more blue the eyes the less the reaction. As the colour went through blue-grey, green, hazel, light brown, and dark brown so the reaction to pain increased on the average.

The author does not offer an explanation of these results, but it is possible to suppose that there is more to them than a freak coincidence. For instance, though the response to pain no doubt owes much to an individual's biological constitution, it is influenced too by his cultural background. Perhaps the patients with blue eyes were mainly of North European stock, traditionally a phlegmatic race, while those with dark brown eyes may have included many descendants of the supposedly more excitable Mediterranean peoples. It would be interesting to know if medical men pay any attention to colour of eyes when assessing, as they have to every day, the intensity of pain about which patients complain.

[1] Critchley, M., *Brit. med. J.*, 1934, **2**, 891.
[2] Sutton, P. R. N., *Nature (Lond.)*, 1959, **184**, 122.

FLUORIDE IN BONE

Teeth developing in the presence of an optimal amount of fluoride are more resistant to dental caries than those which develop in its absence. The prediction can be made with reasonable confidence that the adjustment of the fluoride content of our drinking-water to a level of 1 p.p.m. could result in a lowering of the incidence of dental caries by 40%–60%. A few communities in Britain have drinking-water containing this amount of fluoride and enjoy thereby a lowered incidence of dental caries. Three local authorities have artificially adjusted the fluoride content of their water supplies to the optimal level, and dental examinations are being carried out to determine the extent of the benefit which may be expected in this country.

Fluoride normally accumulates in the skeleton with increasing age, and excessive consumption of fluoride may result in pathological changes in bone. A recent study by D. Jackson and S. M. Weidmann[1] on the fluoride content of human bone in relation to age and water supply is of interest in this respect. They have studied three areas in England—West Hartlepool (1.9 parts per million of fluorine in drinking-water), South Shields (0.8 p.p.m.F), and Leeds (less than 0.5 p.p.m.F). In all areas the fluoride content of cancellous bone from the 6th rib increased with age up to a maximum value at 50–60 years. The absolute amounts of fluoride accumulating in the bone samples were greatest in those from West Hartlepool, least in those from Leeds. There is no evidence to suggest that there are likely to be any pathological bone changes among people living in these areas. In Leeds the bone specimens contained more fluoride than has been reported in bones from areas of low fluoride in the United States. The authors postulate that this difference may be due to the greater consumption of tea in Britain, for tea contains more fluoride than most foodstuffs, and an average cup of tea contains about 1 p.p.m.F. Leeds water is said to contain less than 0.5 p.p.m.F, which the authors refer to as virtually free from fluoride, though since some samples

[1] Jackson, D., and Weidmann, S. M., *J. Path. Bact.*, 1958, **76**, 451.

of water presumably had values approaching 0.5 p.p.m.F this may be one of the factors contributing to the fluoride in the Yorkshire bone. The fluoride content of the water in South Shields is 0.8 p.p.m., but it was for many years 1.2 p.p.m. Hence, say Jackson and Weidmann, fluorine values of rib bone in this area are characteristic of those in a tea-drinking community whose water had been fluoridated to the optimal level. They conclude that, in such a tea-drinking community living in a temperate zone, the fluoridation of drinking-water to the extent of 1 p.p.m. will not enable bone to accumulate fluoride to a toxic level.

This study is of value in allaying the fears of those who feel that the continuous consumption of a fluoridated water containing 1 p.p.m.F may lead to pathological changes in bone. It confirms that the accumulation of fluoride by bone is a normal occurrence. Fluoridation of drinking-water as prophylaxis against dental caries will not lead to pathological changes in bone.

NORMAL WEIGHT IN INFANCY

The standards of normal weight in infancy which have for long been in general use in infant-welfare centres in Britain are based on data collected many years ago. Since then, as surveys have shown, both infants and older children have become heavier and taller, and at the request of the British Paediatric Association the Ministry of Health has been conducting a large survey for the past few years in order that up-to-date standards of normal weight in infancy could be prepared. The committee responsible for this survey has now reported.[1]

The work began in 1949, and altogether 17,308 normal healthy infants attending welfare centres in eleven areas in England and Wales were enrolled in the survey. Each child remained under observation until it reached the age of 3 years. The average birth-weight was 7.53 lb. (3.42 kg.) for boys and 7.21 lb. (3.27 kg.) for girls. The greatest proportion of low birth-weights occurred among the first-born or early-born children of parents in the unskilled classes and the greatest proportion of high birth-weights occurred among the later-born children of parents in the professional and managerial classes.

Between birth and 3 years of age four phases of growth were distinguished: first, relatively variable growth during the first four weeks of life; secondly, a rapid increase to the age of 16 weeks, when the average weight of boys was 14½ lb. (6.58 kg.) and of girls 13¼ lb. (6 kg.); thirdly, a gradual increase to the age of 16 months; and, finally, a fairly uniform rate of growth until the age of 3. At 1 year of age the average weight of boys was 23 lb. (10.44 kg.) and of girls 21½ lb. (9.76 kg.).

The gain in weight from birth to 3 years was largely but not entirely independent of birth-weight: smaller babies grew more quickly than larger babies in their first few months, but later the trends were reversed. The rate of growth varied with the season of the year, but the seasonal pattern changed with age. Thus, up to the age of 3 months, infants born in April to July gained more than those born in November to January. During the first year of life growth was greatest in the summer (April to September), but during the third year growth in April to June was less than in any other quarter, though the greatest growth still occurred in the quarter July to September. Gain in weight after birth was greater for bottle-fed than breast-fed infants and for children of the professional and managerial classes than of the unskilled classes.

The report contains standard curves both of attained weights and of gain in weight from birth to 3 years, and also a table setting out the lower limits which might be used as a practical guide in the assessment of an infant not gaining weight satisfactorily. Medical officers of infant-welfare centres, in particular, will be glad to have these up-to-date figures.

[1] Ministry of Health Reports on Public Health and Medical Subjects, No. 99, *Standards of Normal Weight in Infancy*, 1959. H.M.S.O., London. Price 2s. 6d.

RADIOACTIVE CORPSES

The Ministry of Health has published[1] the recommendations of a panel set up by the Radioactive Substances Advisory Committee to consider the rather macabre problem of the disposal of radioactive corpses. This matter has nothing to do with civil defence against nuclear weapons. It is concerned with the possible danger to undertakers, embalmers, and others who may have to handle the corpses of patients who have received large therapeutic doses of radioactive isotopes. The recommendations make it plain that patients who have received only small "tracer" doses of radioactive substances for diagnostic purposes present no hazard whatsoever. Only three isotopes—^{32}P, ^{198}Au, and ^{131}I—are normally given in large enough quantity to make precautions of this particular kind necessary at all. The recommendations specify the maximum amounts of each of these substances which may be considered entirely safe from the point of view of the embalming, post-mortem examination, or cremation of corpses. The panel recommends that when a patient who has received a therapeutic dose of radioactive material is discharged from hospital his general practitioner should be informed and given any detailed advice about the precautions necessary in the event of the patient's death. Responsibility for advising on the radiation problems associated with the disposal of radioactive corpses is laid on the hospital physicist, who is the person best able to assess the amount of radioactive material remaining in the body and the dose of radiation which anybody handling the body might receive.

Since the risks which these recommendations are designed to eliminate apply principally to undertakers, embalmers, and other persons not employed in the Health Service, it is to be hoped that suitable steps will be taken, possibly through the appropriate professional organizations, to make the recommendations known to the people concerned.

[1] *Mon. Bull. Minist. Hlth Lab. Serv.*, 1959, **18**, 122.

British Medical Association

JOINT ANNUAL MEETING WITH THE CANADIAN MEDICAL ASSOCIATION, EDINBURGH, 1959

SUMMARY OF PROCEEDINGS

THE SECTIONS

SECTION OF ANAESTHETICS

Tuesday, July 21

Too Few Skilled Anaesthetists

With the joint president of the Section, Dr. R. A. GORDON (Toronto), in the chair, Professor E. A. PASK (Newcastle upon Tyne), in a paper entitled "Spreading it Thinner," suggested there were not always enough skilled anaesthetists to go round. Administrators might seek the cheapest standard of treatment consistent with satisfying articulate public demand. As alternatives to developing moderate skill in many doctors by rapid training, one might seek new agents or techniques that could safely be used by persons of limited skill, or "automatic anaesthesia," relying on machines to replace skilled men.

Hypothermia and the Foetus

Dr. S. L. VANDEWATER (Toronto) read a paper on "Observations on the Foetus During Experimental Hypothermia." About 50% of ruptured cerebral aneurysms occurred in women of child-bearing age, and since hypothermia was used in operation on these cases its effect on the foetus was important. From experimental work on pregnant ewes Dr. Vandewater concluded that well-conducted anaesthesia and hypothermia were safe for the foetus. However, maternal respiratory acidosis, hypoxia, or hypotension due to vascular dilatation during rewarming would lead to foetal distress.

Conservative Care of Head Injuries

Dr. A. R. HUNTER (Manchester) discussed the role of the anaesthetist in the conservative care of head injuries. A daily physical examination of the chest was advisable: this would also indicate when tracheotomy was necessary. An indwelling stomach-tube allowed the maintenance of a correct fluid balance. The anaesthetist could also, if necessary, supervise the control of pyrexia with hypothermia, and advise suitable sedatives to allay restlessness in the presence of a raised intracranial pressure.

Anaesthesia for the Ambulant

With the joint vice-president, Dr. H. R. YOUNGMAN (Cambridge), in the chair, Dr. A. TOM (Cheltenham) discussed the limitations enforced on anaesthesia by "ambulant" patients in casualty surgery and chair-side dentistry. Deploring hypoxia and its consequent dangers, he described the use of nitrous oxide with approximately atmospheric concentrations of oxygen.

Head and Neck Surgery

Dr. A. B. NOBLE (Montreal) spoke on certain aspects of anaesthesia for surgery of the head and neck. Unfortunately general anaesthesia often caused respiratory depression with a consequent rise in carbon-dioxide levels. Dr. Noble advocated premedication with pethidine, chlorpromazine, and promethazine, followed by general anaesthesia. Spontaneous respiration with a non-return-valve system was superior to other techniques he had tried, and halothane a better adjunct to nitrous oxide than other volatile agents. Regional and topical analgesia were often helpful, especially when preliminary tracheotomy or intubation was necessary. A head-up posture assisted venous drainage, and post-operative nursing in this position was no less important than during the operation. Dr. Noble concluded by recommending a constant watch for the two most serious complications likely to be met with—disturbance of the carotid-sinus reflex and accidental tension pneumothorax.

E.E.G. in Very Light Anaesthesia

Dr. J. CLUTTON-BROCK (Bristol) spoke on brain rhythms and photic stimuli in very light anaesthesia. He said that nitrous oxide with adequate oxygen was the least toxic but also the weakest anaesthetic agent known, and when it was used with a muscle relaxant objective evidence of unconsciousness would be helpful. A rhythmically flashing light had a greater effect on the cortex than a steady light, and this stimulus could be applied to lightly anaesthetized subjects. It was found that response to it disappeared in unconsciousness produced by nitrous oxide and oxygen. This technique could be used to investigate the mechanism of very light anaesthesia and to assess clinical signs usually attributed to too-light anaesthesia.

Wednesday, July 22

Obstetrical Anaesthesia in Canadian Teaching Hospital

With the joint president, Dr. JOHN GILLIES (Edinburgh), in the chair, Dr. R. A. GORDON (Toronto) said that at the Toronto General Hospital a qualified anaesthetist attended every delivery, and almost 25,000 anaesthetics had been given during the past seven years in obstetric cases. In 1957 there were no maternal deaths, and the corrected foetal mortality rate was 19 per 1,000. Nitrous oxide and oxygen, with or without trichlorethylene, was given for 50% of vaginal deliveries. Local analgesia, and in particular lumbar epidural block, was used in a further 40%. Epidural block had practically replaced spinal analgesia for caesarean section. This was justified by the results, for only seven non-fatal cases of aspiration of vomit had been recorded during the period under review.

Sense of Proportion

Dr. H. H. PINKERTON (Glasgow) spoke on the need for a sense of proportion in anaesthetic training. Orthodoxy had its place, but it should not prevent the employment of improved means to achieve improved ends when it benefited the patient. Hypotension was a valuable technique in some circumstances, but the post-operative complication rate could be as high as 1 in 31. The glamorous techniques of extra-corporeal circulation, hypothermia, hypotension, etc., were not necessarily applicable to the ordinary patient. Trainees must assess these methods properly, and eschew sensationalism, having been drilled first in fundamentals.

Epidural Anaesthesia for Spinal Surgery

Dr. D. MATHESON (Vancouver) spoke on epidural anaesthesia for lumbo-spinal fusion and laminectomy. The results of using epidural block, subarachnoid block, and general anaesthesia were compared, with special reference to loss of blood. In laminectomy alone there was little to choose between them. In laminectomy accompanied by spinal fusion, a markedly lower loss of blood occurred under epidural block. Bleeding increased disproportionately when the operation time exceeded two hours, was aggravated by superimposed general anaesthesia, and was greatest under nitrous oxide, oxygen, and halothane. The results were not influenced by the posture of the patient. Dr. Matheson considered epidural block with 2% lignocaine and 1:300,000 adrenaline (average dose 20 ml. injected at L2–3 or L3–4) an ideal anaesthesia for operations on the lumbar spine, except in the presence of new growths and infection.

Analysis of Respired Gases

With the joint vice-president, Dr. M. W. BOWERING (Regina) in the chair, Professor R. F. WOOLMER (London) read a paper on new methods of analysing respired gases. An anaesthetist should know the composition of a gas mixture presented to a patient. Ideally, there should be a continuous measure of all components. Separate analysis of the inspired and expired gas mixtures would provide additional information. Gas chromatography might be developed to make continuous recording possible, and thus eliminate guesswork—which should no longer be accepted. A single measurement by chromatography took about ten minutes, and this time must be reduced if the method was to become of practical value.

Sensory Thresholds in Light Anaesthesia

In speaking about sensory thresholds in light anaesthesia, Professor J. G. ROBSON (Montreal) referred to John Snow's "second stage of narcotism," characterized by amnesia and analgesia. A similar state could be caused by the inhalation of 40% nitrous oxide and 60% oxygen. Mixtures of nitrous oxide and oxygen, inhaled by volunteers, reduced the rate of learning simple problems. Impairment of memory was similar to that in subjects with temporal lobe lesions. It was hoped that further experiments might lead to a better understanding of the mechanism of amnesia.

SECTION OF ANATOMY AND PHYSIOLOGY

Tuesday, July 21

Somatic Stability in Newborn

The chair was taken in succession by the joint presidents of the Section, Professor J. C. B. GRANT (Toronto) and Professor R. WALMSLEY (St. Andrews). The themes of biological stabilization and development linked the four papers presented.

Professor R. A. MCCANCE (Cambridge), speaking on "Somatic Stability in the Newborn," said that the foetus possessed regulatory mechanisms from its first existence. There were, however, special risks to stability in the newborn period. The most urgent was failure of gas exchange. In the clinical management of asphyxia, intravenous sodium bicarbonate and glucose were needed first; these would lower the serum potassium. Oxygen was the next need. Re-warming should be delayed until asphyxia had been overcome.

Professor McCance went on to describe how recent research has thrown light on the means by which the newborn animal maintains internal stability.

Regulation of Blood Calcium

Professor D. H. COPP (Vancouver) spoke on the regulation of blood calcium. The calcium in blood was only a small part of the calcium in the body; equilibration with the large pool of calcium in bone was the first factor which buffered disturbances of blood calcium. A second method of regulation was excretion of calcium by the kidneys, if the level in the blood rose. The parathyroid hormone was the third means of control. In the absence of the parathyroid glands the blood calcium level was low and stabilization was poor.

Iron in Mammary Glands

Professor H. E. RAWLINSON (Edmonton, Alberta) discussed the iron content of the mammary glands. A need existed for assessing the activity of mammary gland tissue. Histological studies had shown the presence of large amounts of iron in the alveolar tissue of the gland in rodents, though not normally in man. Much more iron was present in the glands of mice which had bred than in virgin mice. The iron content rose during early pregnancy, fell in late pregnancy, and rose again soon after the cessation of lactation. Among different strains of mice the iron content was higher in those with a high incidence of mammary cancer. Suppression of lactation caused a significant and long-lasting increase in iron content.

Anatomy of the Newborn

Professor R. WALMSLEY (St. Andrews) described the anatomy of the newborn child and presented a series of colour slides illustrating some of the peculiar anatomical features of the newborn human. He concluded by pointing out that in none of the structures discussed was the newborn child a miniature of the adult; and that in general the structures which developed early were those needed early in life.

On July 21 and 22 members of the Section enjoyed a number of interesting demonstrations in the Edinburgh University Departments of Anatomy and Physiology.

SECTION OF CARDIOLOGY

Tuesday, July 21

Symposium on Coronary Artery Disease

With Dr. D. EVAN BEDFORD (London) in the chair, Dr. PAUL WOOD (London) was the first speaker in the symposium on coronary artery disease. He discussed subacute coronary insufficiency, which occurred when the coronary circulation did not meet adequately the demands of the cardiac muscle at rest, but was sufficient to prevent cardiac infarction. Such a condition was termed subacute when its duration was between a few weeks and six months, but it could continue into a chronic phase, when it might last one year or more. The more chronic cases, however, were rare, forming only 5% of the speaker's 150 cases.

Subacute Coronary Insufficiency

The majority of patients developing subacute coronary insufficiency gave a previous history of ischaemic heart disease, but one-fifth of them developed this state *de novo*. Attacks of pain in subacute coronary insufficiency might last days and yet there was no laboratory evidence of infarction. The typical electrocardiographic pattern showed widespread depression of the ST segment, without pathological Q waves or frank inversion of the T wave. The onset of this syndrome might be abrupt, with no apparent reason, when it was probably due to coronary thrombosis without infarction. In other cases it was generally due to progressive coronary atherosclerosis. One-fifth of patients developed cardiac infarction within two months of the onset of subacute coronary insufficiency. Treatment with anticoagulants had greatly improved the prognosis.

Electrocardiographic Diagnosis

Dr. H. N. SEGALL (Montreal) said that coronary artery disease could be present with a normal electrocardiogram, while minor abnormalities in the electrocardiogram could be caused by tobacco, digitalis, quinine, quinidine, as well as by coronary disease. In doubtful cases repeated serial electrocardiograms should be taken. The exercise electrocardiogram had been introduced as a further aid to diagnosis, but in this also the wide range of variability of the normal gave rise to confusion. The speaker warned against the danger of iatrogenic coronary artery disease founded on electrocardiographic misinterpretation. He said that in a recent test of observer variation, in which 20 observers had reported on 100 graphs, a wide discrepancy was found.

Management of Acute Myocardial Infarction

Dr. A. RAE GILCHRIST (Edinburgh) spoke about some problems in the management of acute myocardial infarction. Diagnosis presented the first problem, and he stressed the

accuracy of electrocardiographic interpretation in his department in relation to patients coming to necropsy, where the cardiographic diagnosis was confirmed in 94% of cases. The second problem was that of home or hospital care. He favoured institutional treatment for the great majority, but account had to be taken in individual cases of the age, the distance of the patient's home from the hospital, the need for special laboratory examinations, and the severity of the attack.

It was well known that firm scar formation after cardiac infarction occurred in about six weeks, but this should not influence the period of bed rest in cardiac infarction too greatly. Three weeks was probably sufficient in most cases: more prolonged bed rest carried with it many dangers—general deterioration in morale, loss of muscle tone, stiffness in the joints, and deep leg vein thrombosis. He did not favour armchair treatment as an alternative to treatment in bed, since it was a tiring posture for the patient. Early physiotherapy should be given in all cases, and most patients should be out of bed after three weeks and out of hospital after four. Advice to the patient returning to work should be optimistic and encouraging: "Do as much as you can short of producing symptoms."

Ventricular Septal Defects

With the joint president, Dr. H. N. SEGALL in the chair, two short papers were read. Dr. J. E. GIBBONS (Montreal) discussed the management of infants with ventricular septal defect. He said that no firm advice could yet be given about the best age for surgical treatment. It was probably wisest not to attempt surgery before the age of one year, since the mortality over this period with adequate medical care was low—in the region of 5%. Surgical treatment could be more safely undertaken between the ages of 2 and 3 years, with a surgical team experienced in cardiac surgery in infants. Only the exceptional case needed urgent surgical treatment in the first year of life.

X-ray Changes in Heart Disease

Dr. PETER J. KERLEY (London) discussed lung changes in heart disease with special reference to the pulmonary lymphatics. The linear pattern, known as Kerley's lines, seen especially clearly in the costophrenic angles in a postero-anterior film of the chest of a patient with heart disease, was due to interstitial oedema, the lines following the known paths of the pulmonary lymphatic system. They might be indicative of a raised pulmonary venous pressure, but were not directly related to a raised pulmonary arterial pressure, although both conditions commonly coexisted in severe mitral stenosis. They could occur in other diseases which caused lymphatic obstruction, such as carcinomatosis and some forms of pneumoconiosis. They were never seen in a normal *x*-ray picture of the chest and were therefore of great diagnostic importance.

Wednesday, July 22

Treatment of Hypertension

With Dr. RAE GILCHRIST, P.R.C.P.Ed. (Edinburgh), a joint president of the Section, in the chair, two problem cases were presented for discussion and diagnosis to a panel of six, Dr. R. W. D. TURNER (Edinburgh), Professor I. G. W. HILL (Dundee), Dr. D. EVAN BEDFORD (London), Dr. PAUL WOOD (London), Dr. A. J. KERWIN (Toronto), and Dr. H. N. SEGALL (Montreal).

The Section then turned to a discussion on the treatment of hypertension, and Dr. JACQUES GENEST (Montreal) took the chair. Professor M. L. ROSENHEIM (London) stressed the importance of unilateral renal disease in the aetiology of severe hypertension. The most useful test in diagnosing this condition was an intravenous pyelogram. The finding of a unilateral small kidney that was functioning promised a good therapeutic result after nephrectomy. When the small kidney was non-functioning, relief of hypertension after nephrectomy was less certain. A unilateral small kidney was due either to pyelonephritis or to ischaemia from arterial stricture or obstruction. An aortogram was often helpful in recognizing the ischaemic kidney.

Sir GEORGE PICKERING (Oxford) was less enthusiastic about the results of unilateral nephrectomy, since in chronic bilateral pyelonephritis the kidneys were often unequal in size and removal of the smaller kidney would not necessarily benefit the patient's hypertension. He also felt that, in view of the known risks of an aortogram, one should be very cautious before having recourse to this test, which should be reserved for the young patient with severe hypertension and unequal kidneys.

Dr. M. NICKERSON (Winnipeg) advised needle biopsy of the kidney to help assess renal function in such patients, but Dr. GENEST doubted whether the information obtained justified the risk involved. He also said the relief of hypertension following unilateral nephrectomy had been found to be sometimes only temporary, hypertension recurring after two years or more.

Bretylium Tosylate

There followed a discussion on the medical treatment of hypertension. Professor M. L. ROSENHEIM discussed his experience with the use of the new drug "darenthin" (bretylium tosylate), which specifically blocked sympathetic nerves without inhibiting the parasympathetic nervous system. The early trials suggested it was possible to obtain marked postural hypotension with this drug, without side-effects on the eye or bowel. Dr. J. A. LEWIS said there was no doubt that if a 0.5 g. sodium diet was conscientiously adhered to a satisfactory drop in diastolic blood pressure could be achieved in many patients. A more promising line of treatment was the combination of ganglion-blocking agents with chlorothiazide or hydrochlorothiazide. Professor W. D. M. PATON said that the effect of adding chlorothiazide to treatment with ganglion-blocking agents was like doing a small venesection. The panel generally agreed that this combination of drugs in the medical therapy of hypertension was proving useful.

Sir GEORGE PICKERING said that malignant hypertension should be regarded as a medical emergency. Professor ROSENHEIM agreed that it was important first to get the blood pressure under control, but stressed that a treatable cause should then be carefully sought, such as a phaeochromocytoma or renal disease.

Lastly, Dr. LEWIS discussed the treatment of mild benign hypertension, in which there were no symptoms. It was important to reduce obesity. The sedative effect of phenobarbitone was probably preferable to that of reserpine in such patients, in view of the frequency of depression after reserpine. Dr. GENEST believed, however, that reserpine seldom caused depression, provided it was used in small doses (under 0.5 mg. daily). In relation to the treatment of hypertension in patients of 65 years or older, where the rise in pressure was primarily systolic, there was general agreement that no treatment was required. In conclusion Dr. Genest stressed the importance of psychological factors in the sudden onset of hypertension.

SECTION OF CHEST DISEASES

Thursday, July 23

Management of Chest Infections

With Dr. J. D. ADAMSON (Winnipeg), a joint president, in the chair, Professor J. W. CROFTON (Edinburgh) introduced a symposium on the management of chest infections by emphasizing the importance of liaison between clinicians and bacteriologists. Virological diagnosis was often in retrospect. The virologist must develop techniques which would help the clinician in early diagnosis, who could not wait for full bacteriological investigation before treating

the patient; he had to act quickly and be prepared to correct his treatment when laboratory results became available.

Treatment of Pneumonia

Dr. F. S. GRÉGOIRE (Montreal), discussing the treatment of pneumonia, said that full clinical, radiological, and laboratory investigation should be carried out before treatment began. Specific treatment should continue until all signs of infection had gone. In pneumococcal and streptococcal pneumonia penicillin was the most useful drug, though sulphonamides were highly effective and erythromycin almost equally good. The other broad-spectrum antibiotics were slightly inferior. In the treatment of staphylococcal pneumonia it was best to use two drugs to which the organism was sensitive. If penicillin was given, large doses, such as 50 million units daily, might be required. Vancomycin was proving valuable in resistant cases. Symptomatic treatment was the treatment of choice in viral pneumonias, but antibiotics had a place in suppressing secondary infection.

Bronchitis

Dr. A. BRIAN TAYLOR (Birmingham) said that the management of patients with bronchitis was difficult, since infection, atmospheric pollution, allergy, and heredity all played a part. The common cold and influenza could initiate bronchitis, but secondary bacterial invasion might perpetuate it. Although secondary infection could be controlled by antibiotics, symptoms persisted after bacteria had been eliminated from the sputum. The rapid rise in pulmonary arterial pressure during episodes of bronchial infection led to right-heart failure. Accumulated mucus in the bronchial tree caused narrowing of bronchi: treatment with trypsin and aerosols did not satisfactorily overcome this obstruction. When there was severe retention of mucus, tracheotomy, lavage, and oxygen therapy could be life-saving.

Rapidly spreading bronchitis suggested an allergic factor and was an indication for steroid therapy. Short, intensive, and limited courses of steroids served best, and antibiotics should be given at the same time. Vaccines helped in reducing allergy; autogenous vaccines were preferable to stock preparations.

Anoxia in Chest Infections

In describing the effects of anoxia in chest diseases Dr. T. SIMPSON (London) said that an impaired mental state indicated cerebral anoxia and was a bad prognostic sign. Papilloedema was a reliable sign of oxygen lack. Increased dyspnoea, tachycardia, drowsiness, and tremor of the hands signified oxygen deficiency. In treatment, it was vital to relieve oxygen deficiency at an early stage. The risk of carbon-dioxide retention could be avoided if oxygen was given slowly or intermittently. Although tracheotomy was not often required, there should be no hesitation in resorting to this procedure when necessary.

Empyema

In the regrettable absence of Professor F. G. KERGIN (Toronto), through illness, Sir RUSSELL BROCK, joint president, read Professor Kergin's contribution on the treatment of empyema. Empyema was no longer a common disease, but it was often a terminal complication in older patients. Causal organisms were found only in about three-quarters of patients. Where the infection was pneumococcal aspiration of the empyema combined with antibiotics was usually successful. Streptococcal empyemata required draining. If there was a bronchopleural fistula open drainage was needed. In most cases of empyema it was best to try daily aspirations and antibiotics. Local instillation of proteolytic agents was of no value, but when thick pus was present irrigation with normal saline helped. Decision about surgical treatment could be made after two weeks, at which time surgical drainage was quite safe. Biopsy of the parietal pleura should be carried out to exclude carcinoma and tuberculosis. Rib resection and drainage still had an important place in treatment, though decortication might be necessary in chronic empyemata and in chronic haemothorax.

In the discussion Sir RUSSELL BROCK (London) warned that long-continued aspiration of empyema could be dangerous. Decortication was indicated when there were widespread collections of pus in the pleura, when there were loculated irregular collections of pus, when the empyema was large, and when there was doubt about the outcome.

Friday, July 24

Sarcoidosis

With Sir RUSSELL BROCK (London), joint president of the section, in the chair, Dr. A. ANGLIN (Toronto) read a paper on sarcoidosis. The aetiology, he said, was uncertain, but its common association with tuberculosis suggested a tuberculous origin. It was sometimes possible to trace a gradual change from sarcoidosis to flagrant tuberculosis. Tubercle bacilli were not found in sarcoid lesions, and injection of sarcoid tissue into animals did not produce tuberculosis.

A geographical survey of the condition in the U.S.A. had revealed an endemic zone along the eastern coast, coinciding with the distribution of pine forests. There seemed to be a definite link between pine pollen and sarcoidosis. Pine pollen had a certain chemical similarity to the tubercle bacillus, and, when injected, it could produce a sarcoid-like reaction. Pine pollen had been found in the sputum of some patients with sarcoidosis.

It had recently been shown that the negative tuberculin test commonly found in sarcoidosis often changed to a positive when patients were given steroid treatment. This might prove to be valuable in diagnosis. Steroids provided the only satisfactory form of treatment for sarcoidosis.

In discussion Professor J. W. CROFTON (Edinburgh) said that he had been unable to confirm the association of pine forests with sarcoidosis in Edinburgh, where most patients were town dwellers. It was interesting that American negroes often developed sarcoidosis whereas African negroes apparently did not. Dr. BRIAN TAYLOR (Birmingham) drew attention to the occasional finding of sarcoid tissue in curettings from the uterus. Dr. I. W. B. GRANT (Edinburgh) had found it necessary to continue steroid therapy for many years, since relapses occurred when treatment was stopped.

Smoking and Lung Cancer

Dr. C. R. LOWE (Birmingham) summarized the facts relating to the association between smoking and lung cancer. It was in the interpretation of these facts that differences of opinion had arisen. It might be argued that it was lung cancer that caused people to smoke. The suggestion that some precancerous state caused an irritation inducing a desire to smoke could be dismissed. It was also possible that bronchogenic carcinoma and smoking were related through a common cause—for example, an individual genotype. Thus a person might inherit a predisposition both to lung cancer and to smoke cigarettes. There was evidence that personality traits had some bearing on smoking habits, and it was likely that the genotype was important in cancer of the lung. There was, however, no evidence whatever to suggest that there was a genotype which exhibited both proneness to lung cancer and a desire to smoke. On the other hand, there was a great weight of collateral evidence to support the hypothesis that cigarette smoking was a direct cause of lung cancer.

Bronchiectasis

Mr. R. J. M. MCCORMACK (Edinburgh) surveyed the surgical treatment of bronchiectasis in the light of experience

from 252 consecutive patients treated by resection in Edinburgh. Claims had been made that antibiotics had replaced surgery in the management of bronchiectasis, but this was not true. Operative mortality was low. There had been no deaths in the last 120 patients undergoing operation. Post-operative complications had become rare. Three-quarters of the patients treated by resection were able to return to a full life without respiratory symptoms. In only about one-tenth of the patients had the results been disappointing.

In the ensuing discussion Professor P. R. ALLISON (Oxford) said that removal of an infected bronchiectatic area would sometimes help the patient with chronic bronchitis. Sinus infection often aggravated bronchiectasis, but Mr. McCormack said he had found treatment of sinus infection of little help.

Cough and Cancer

Professor J. D. ADAMSON (Winnipeg) described an investigation into the incidence of bronchial carcinoma in patients with a chronic cough. It had been asserted that almost any sort of bronchial irritation would give rise to bronchial carcinoma. To test the validity of this suggestion an investigation had been carried out by comparing the case histories of 500 Canadian pensioners dying from bronchial carcinoma with an equal number of controls of similar age. The results clearly showed that chronic cough was no more common in patients with bronchial carcinoma than in those dying from other cause.

SECTION OF CHILD HEALTH

Monday, July 20

Neonatal Hyperbilirubinaemia

With the president of the Section, Professor STANLEY G. GRAHAM (Glasgow), in the chair, Dr. A. E. CLAIREAUX (London) opened a discussion on jaundice in the newborn. This was common, as 40% of newborn babies developed bilirubin levels of over 4 mg./100 ml. The term physiological should be rejected, as neonatal hyperbilirubinaemia might be not only dangerous but fatal. Bilirubin was not toxic to the brain once it was conjugated by transferase in the liver to bilirubin glucuronide. The danger of kernicterus was therefore mainly from non-obstructive jaundice, especially from untreated haemolytic disease, from liver immaturity in premature babies, and occasionally from congenital spherocytosis and congenital familial non-haemolytic jaundice. Obstructive jaundice was not usually dangerous to the brain.

Dr. W. WALKER (Newcastle upon Tyne) said that haemolytic disease was the commonest cause of dangerous jaundice. It affected five to six per thousand live births. With adequate diagnosis and early treatment the death rate should be 0.2 per thousand, but the national figure was still 0.5. Of the 350 yearly deaths 200 were probably avoidable.

In Newcastle, the survival rate in 974 affected live-born infants given early exchange transfusion was over 96%, and no deaths from haemolytic disease occurred in 402 babies not treated by exchange transfusion. The keyword was antenatal prediction, which made hospital delivery possible in 90% ; severity could be predicted on cord values, and, where indicated, early exchange transfusion carried out before jaundice occurred. Any baby developing jaundice within the first day should be regarded as having haemolytic disease until proved otherwise.

Dr. J. P. BOUND (Liverpool) spoke on hyperbilirubinaemia in premature babies. With the reduction in dosage of "synkavit," kernicterus of prematurity was uncommon. Only two deaths from kernicterus had occurred among about 4,000 premature infants born in March, 1958, and surveyed in a recent British national inquiry (Perinatal Mortality Survey). About 4% of 350 premature infants in his area had developed bilirubin levels over 18 mg./100 ml., but none died of kernicterus. Only one received exchange transfusion. No sequelae had so far been reported. He had now raised his threshold for transfusion from 18 to 30 mg./100 ml., except with a history of birth or postnatal hypoxia, or if lethargy, irritability, or difficulty in feeding developed.

In reply to Professor J. L. HENDERSON (Dundee), Dr. WALKER said that only 11 out of 250 recent cases of haemolytic disease in Newcastle were due to antigens other than Rh anti-D. Professor J. D. HAY (Liverpool) asked about premature induction in affected pregnancies, and Dr. WALKER said that this might eventually prove most useful in first affected pregnancies, in which over 80% of foetuses were still alive at 35 weeks' gestation.

Reappraisal of School Health

With Professor R. W. B. ELLIS (Edinburgh), a vice-president of the Section, in the chair, Professor H. MEDOVY (Winnipeg) gave a short paper on recent experiences in Winnipeg, a city with 50,000 children where close liaison existed between paediatric service and city health authority. Routine school medical examinations had been given up, as chronic disease had been discovered already in any pre-school child or infant at welfare clinics, and nearly 70% of schoolchildren received examination by their own physician. Moreover, it was impossible to examine adequately 30 to 50 schoolchildren in two hours. Instead, new cases of ill-health and physical handicaps, such as deafness and defective vision, were reported to the medical officers individually as they were noticed. Teachers were kept informed by regular bi-weekly bulletins and discussion groups. A medical screening questionary was under trial for completion by parents when the child was 12 years old.

Routine visual tests were carried out by class teachers every year, with special visual examination at three-yearly intervals and whenever scholastic progress was poor. Audiometry was done by technicians at 9 to 10 years. By these methods special cases could be given adequate time for examination.

Regular progress reports of handicapped children were forwarded by school medical officers to their physicians, with whom close liaison was kept.

A short communication was given on the prognosis of asthma in childhood by Dr. C. COLLINS-WILLIAMS (Toronto). He stressed the frequency of childhood asthma in Canada and the benefits of a planned regime by which 88% of 152 asthmatic children had been improved on a four-year follow-up.

Wednesday, July 22

Staphylococcal Infection in Newborn Infants

With Professor J. L. HENDERSON (Dundee) in the chair, Dr. J. O. FORFAR (Edinburgh) opened a discussion on staphylococcal infection in newborn infants. He said that the incidence of pus-producing or indurated inflammatory lesions in Edinburgh maternity units in 1957–8 was 12%, and a similar incidence had been reported in London and Bristol. This represented 60,000 affected infants yearly in England and Wales and 8,000 in Scotland. Infections were usually mild, such as conjunctivitis (60%), skin pustules (20%), and paronychia (8%), but in epidemics up to 50% of lesions might be severe. The hospital staphylococcus showed increased antibiotic resistance—in his unit 72% were resistant to penicillin—and gave a high carrier rate, intranasal swabs being positive in up to 30% of mothers, 50% of nursing staff, and 90–100% of infants. Spread was by contact, dust from contaminated articles, and, less commonly, by droplet infection.

Among routine precautions were frequent hand-washing, disposable napkins, special sterilization of blankets, and

separate cot-nursing instead of communal changing-rooms, etc. Hexachlorophane was useful for sterilization of hands and umbilicus.

Infections in Babies Born at Home

Dr. F. J. W. MILLER (Newcastle upon Tyne) dealt with staphylococcal infections in babies delivered at home. In a recent (unpublished) Newcastle investigation, 72 (18%) infants out of 395 consecutive domiciliary births had developed neonatal infection, and produced 90 (29%) out of 309 consecutive hospital births. The overall incidence differed little from that in the survey of 1,000 families in Newcastle ten years earlier, but severe infections were rare in the recent investigation. An examination of the records of 650 consecutive domiciliary deliveries over six years by one practitioner in Newcastle had shown only nine neonatal infections requiring medical attention, with one fatality. Because of resistance to penicillin, chloramphenicol was now the drug of choice in Newcastle for neonatal staphylococcal infections.

Experience in a Surgical Unit

Miss ISABELLA FORSHALL (Liverpool) said that, so far as acute neonatal surgery was concerned, only 15% of 120 "clean" cases had developed staphylococcal infections in a large surgical neonatal unit; the overall mortality of 20% was due mainly to severe malformations. All were given prophylactic antibiotics routinely. Surgical cases with pre-existing staphylococcal infection elsewhere also did well. Minor lesions required immediate antibiotic sensitivity tests.

In the discussion, several speakers noted a decline in acute staphylococcal neonatal lesions in domiciliary practice.

Speech Disorders in Childhood

The first of three papers on the diagnosis and management of speech disorders in childhood was read by Miss E. WHETNALL (London), who spoke on the vital part played by auditory stimuli in normal speech development. Speech defects would develop unless individual afferent auditory impressions were loud enough, repetitive over a long period, and absorbed at the right age for learning and in their correct context. Language training was essential as well as hearing-aids. Children deprived later of acquired hearing by otitis or meningitis formed a rare but important group who required treatment.

Dr. T. T. S. INGRAM (Edinburgh) spoke on the diagnosis of speech disorders. Although facilities were becoming available for speech therapy, diagnosis lagged behind. Audiometry was carried out on all cases. A convenient classification was by the major function of speech to be disturbed—namely, dysphonia; disturbances of rhythm, such as stammering; disorders of articulation, with or without dysfunction of articulatory apparatus; and developmental speech disorder. A special diagnostic clinic, as now used in Edinburgh, had thrown light on many related disorders in children referred for speech therapy.

Dr. W. N. BOOG-WATSON (Edinburgh) spoke on speech training and therapy in the school health service. Speech training for normal children should be a part of the ordinary school curriculum, but it was often neglected both in teachers' courses and, indeed, in medical training. Speech therapists were employed in order to ascertain and treat defects of speech; they should be under the direction of the school health authority.

Friday, July 24

Psychoses in Infancy and Childhood

With Professor J. D. HAY (Liverpool) in the chair, the Section discussed psychoses in infancy and childhood. Dr. K. CAMERON (London) emphasized that juvenile psychosis followed a well-defined pattern. Early developmental history was rarely normal, though the child was not usually backward chronologically. Symptoms generally started at 2 to 3 years, sometimes precipitated by an episode of emotional or physical trauma, such as an accident or a burn. The fully developed picture was that of withdrawal, regression, alteration in motility, diminution of affect and emotional response, and the presence of patterns of thinking, feeling, and actions derived from inner thoughts. Formes frustes occurred in differing degrees. Subsequent progress might be apparent recovery, with or without later adult schizoid trends; partial recovery, with residual brain damage; or deterioration into subsequent adult schizophrenia or even progressive dementia. It could be almost impossible to distinguish between a defective and a deteriorated schizophrenic, but the latter usually had a history of islands of normality, with periods of development and regression.

Family Influences

Dr. W. A. HAWKE (Toronto) spoke on constitutional and environmental factors in aetiology. Two recent Toronto studies, on 50 and 40 autistic children respectively, had both shown a significant tendency toward schizophrenic disturbances in the families. Parents were often very intelligent, with an average I.Q. of over 120, but 80–90% were classed as moderately or severely neurotic or themselves schizoid. They were often singularly unsuccessful in community and family life. Only 25% could form an adequate relationship with therapist or child. Rejection by their autistic child often led to further withdrawal on the part of parents. Therapy had to be directed to improve the relationship between child and parents. Sometimes placement in a foster home or institution was unavoidable.

Treatment

Dr. F. H. STONE (Glasgow) agreed that the results of treating juvenile psychosis were poor, but said that treatment should include support and explanation for parents, with individual psychotherapy for the child when necessary, special educational facilities, and temporary use of sedatives and tranquillizers. Such needs could probably best be met by psychiatric day hospitals, especially in areas such as Glasgow, where cases were increasing and beds were short.

Dr. MILDRED I. POTT (London) stressed that any plan of treatment for psychotic children must take into account stresses and strains on the family, especially on normal siblings. Because of this difficulty community care would not be suitable for some children. Small residential units with special educational facilities would be best for some cases, provided close contact was maintained with the family as part of the treatment of both child and parents.

Dawson Williams Lecture

Mr. DENIS BROWNE chose as his subject "The Logic and Logistics of Paediatric Surgery." He gave a philosophical appraisal of the scientific method in medical inquiry from Francis Bacon to the present day, advocating the observational as well as the experimental approach and outlining the pitfalls of each. The aims of paediatric surgery should be to establish standards without monopolies, to compare achievements in one centre with those in others, and to avoid the boundaries of over-specialization.

SECTION OF DERMATOLOGY

Thursday, July 23

The Skin and Disordered Porphyrin Metabolism

With the joint president, Professor G. H. PERCIVAL (Edinburgh), in the chair, Dr. A. LYELL (Aberdeen) opened a discussion on porphyria. There were the inherited metabolic defects, as seen in congenital porphyria, acute

intermittent porphyria, and protocoproporphyria, and the required porphyria cutanea tarda symptomatica, which was due to liver disease. In acute intermittent porphyria the only skin change was occasional pigmentation. The skin changes in the other types were due to light and were limited to exposed parts. They consisted of erythema and oedema, blisters and scarring and pigmentation, and were thought to be due to increase of porphyrin in blood and tissues from impaired biliary secretion.

Dr. G. HOLTI (Birmingham) spoke on the investigation of suspected cases of porphyria. Small quantities of porphyrins were present in every cell either in the free state or as metal complexes, combined with proteins forming haemoglobin, cytochromes, or catalysts essential to cell metabolism. Diagnosis was based on the excessive production of free porphyrins or their precursors. Normal urine contained up to 200 μg. per litre of coproporphyrin, 30 μg. per litre of uroporphyrin, and up to 40 μg. per 24 hours of the precursors δ-aminolaevulic acid and porphobilinogen. Normal stools contained up to 50 μg. per g. dry weight of copro- and protoporphyrin combined. If liver function was not impaired urinary porphyrin levels might remain normal, even though abnormal quantities were present in the stools. Porphyrins might also be produced in the bowel by bacterial synthesis, but oral antibiotics restored the position to normal. Examination of urine and stools of blood relatives indicated whether the disorder was hereditary or acquired.

Skin Lesions in Reiter's Syndrome

With the joint president, Professor H. A. DIXON (Toronto), in the chair, Dr. R. C. SMITH (Toronto) read a paper on the skin lesions of Reiter's syndrome. It was almost limited to males between the ages of 20 and 40 years, the cause was unknown, and treatment was of limited value. Steroids gave symptomatic relief. The conjunctivitis usually cleared in two weeks, but involvement of the uveal tract might occur. The arthritis might persist for three to six months, but there was a tendency to recurrences.

Local Use of Adrenal Steroids in Dermatology

Dr. G. E. CRAIG (Montreal), reading a paper on this subject, said that the free-alcohol preparations were usually the more effective. Recent research had shown that some absorption did occur from topical applications. Hydrocortisone ointment was useful in all stages of atopic eczema, including the thickened flexural types, but it was of no value in psoriasis except for the seborrhoeic type of eruption occasionally seen in flexures. He had used injection of hydrocortisone effectively in treating the pseudomucinous cysts of fingers, sebaceous cysts, and cystic acne.

SECTION OF GENERAL PRACTICE

Thursday, July 23

The Ageing Population

Under the joint chairmanship of Drs. G. W. IRELAND (Midlothian) and JACK MCKENTY (Winnipeg) the theme of "The Ageing Population and the Community" was discussed.

Dr. MCKENTY introduced the session by giving an account of the College of General Practice in Canada. It had been founded in 1954 and had always had good relations with the Canadian Medical Association, to the extent that it had made the College a gift of 10,000 dollars at its inauguration.

Dr. H. GIBSON HALL (Toronto) spoke of his research into the early features of hypertension in his practice over a period of 26 years. He had found that from the ages of 15 to 19 the blood pressure in any individual tended to be unstable and labile; from 20 to 54 there was a period of stability; this was followed by a labile phase from 55 to 62; and finally in old age the blood pressure was again stable. These findings applied to men as well as women. With old age there was a tendency for the blood pressure to fall by 8–10%. Dr. Hall had observed 514 patients with a family history of hypertension and had noted a progressive rise in blood pressure after the period of stability from 20–54. In 173 other persons without this positive family history there had been no rise in blood pressure. He had found that obesity was definitely related to an unstable and rising blood pressure at a younger age. Emotional factors were often a cause of a rising blood pressure which tended to persist.

Hypertension in the Elderly

Dr. I. H. STOKOE (Edinburgh), speaking on hypertension in the elderly, said that the question of a figure for a "normal" blood pressure was a difficult one. His own criterion for those aged 65–90 was 120 mm. Hg plus half the age. The common form of hypertension in the elderly was the systolic variety, which increased with age, but fell after the age of 80. As a rule symptoms were slight and often related to anxiety. The prognosis was good. Moderation in all things was the advice to give to the patient.

The dangers of over-frequent taking of blood were emphasized in the discussion.

Geriatrics in General Practice

Lord AMULREE (London) considered that "geriatrics" should be a label applied not to "old" persons, but only to those elderly sick with social and economic problems. These problems were four in number: (1) loneliness; (2) neglect, leading to dirt and squalor; (3) lack of domestic help; and (4) lack of food, malnutrition being still appreciable in the elderly. Although home was the best place for the elderly, there had to be beds available for the acute case, social as well as medical. Among the risks of hospitalization in the elderly were death, irreversible confusion, and loss of independence. A hospital with a geriatric service would provide, in addition to beds, an out-patient service, domiciliary visits to assess the home situation, and co-operation with local authority services.

General Practice in the Prairies

Dr. CLARENCE J. HOUSTON (Yorkton, Saskatchewan) gave a most interesting account of the work of a general practitioner in the Canadian prairies. He thought that 90% of illnesses could be managed by the general practitioner alone in his own practice. Approximately 3,000 persons were in his care: he was 40 miles from his nearest medical colleague and 100 miles from the nearest medical centre. In spite of that he fitted his work into a reasonably well planned day with time for thought and leisure. This was possibly explained by the common North American custom of concentrating all the work in the "office" and hospital. Dr. Houston did very few house visits. Most of his work was private practice, although many patients were covered by medical insurance policies. He thought that in his practice there was less morbidity and less malingering than in Britain, where the medical bill was paid by a third party.

Socio-medical Research

Dr. RICHARD SCOTT (Edinburgh) gave a report on various socio-medical research studies carried out at the General Practice Unit of Edinburgh University. There was a rise in doctor–patient consultations with age, a rise that was more apparent in women than in men. A survey of housing standards showed that there was a fall in standards as age advanced, many of the elderly living alone and in

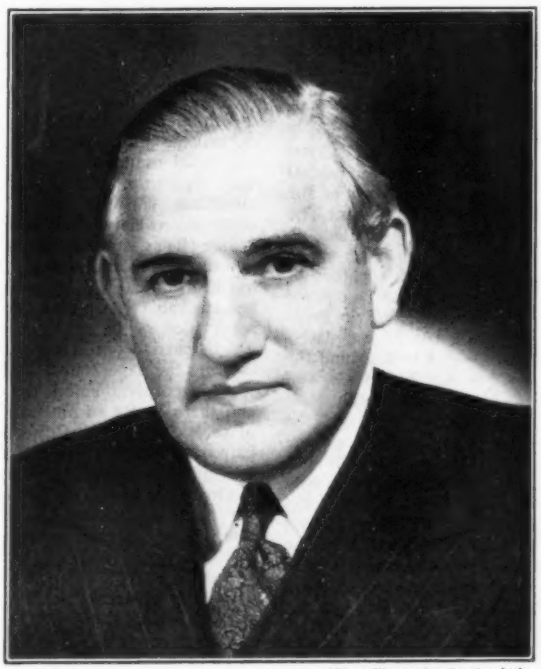
isolation. The importance of socio-economic factors was shown in the high proportion of cases (over 25%) that required some form of social therapy. Emotional instability was noted in 9% of all consultations, and here the peak levels were noted in women between 25 and 50.

In the ensuing discussion concern was expressed by British family doctors over the lack of family responsibility in the care of the elderly. To show that this was by no means a British failing, the same trends were reported by a number of Canadian speakers.

THE ISAAC WOLFSON FOUNDATION

GIFT TO ROYAL COLLEGE OF PHYSICIANS

Last week's princely gift of £450,000 to the Royal College of Physicians will focus the interest and gratitude of the medical profession on the Isaac Wolfson Foundation and its creator, Mr. Isaac Wolfson. Not much so far has been heard publicly about the Foundation, apart from the announcement from time to time of a number of large grants, and no annual report on its activities has yet appeared. Mr. Wolfson is, of course, well known as the managing director of the Great Universal Stores Ltd.



[Fleet Illustrating Service Ltd.
Mr. Isaac Wolfson.

The Foundation was established by Mr. Isaac Wolfson in 1955. At that time there were only four trustees. Lord Nathan, who is also chairman of the Westminster Hospital, was chairman, and the others were members of the Wolfson family—Mr. Isaac Wolfson himself, his wife, and his only son Mr. Leonard Wolfson. The Trust Deed, drawn in the broadest possible terms, made the Foundation's main purpose the advancement of education and health in the United Kingdom and Commonwealth. Three years later the funds were greatly increased and the Foundation was put on a more formal basis by the appointment of a further five trustees, of whom two are medical, and a director. The new trustees are Lord Birkett, Sir Stanford Cade, Lord Evans, Professor A. L. Goodhart, and Sir John Cockcroft. The director is Lieutenant-General Sir Harold Redman. In July, 1958, the Foundation had a capital fund of £6m., mainly holdings in the Great Universal Stores. It has distributed more than £2m. in grants.

Benefactions

To date the Foundation's benefactions have been concentrated in a few selected fields appropriate to its aims: the support of scientific and technological education; the provision of buildings for higher education; youth activities; medical research; and the improvement of medical and nursing services generally. Like other charitable foundations, the Isaac Wolfson Foundation seeks the worthy project for which public funds are not forthcoming. It gives, on the whole, in large sums so that the effect may be decisive, and, where practicable, to objects of national rather than sectional importance. The gift making possible the building of a new home for the Royal College of Physicians is by far the largest grant yet made by the Foundation. Other large grants in the medical field have been £250,000 for the Westminster Hospital School of Nursing, £184,000 to the Institute of Psychiatry (London University), £150,000 to the British Empire Cancer Campaign, £125,000 towards the expansion of the Postgraduate Medical School of London, and grants of £50,000 and £25,000 respectively to the Royal National Institute for the Blind and the British Council for the Welfare of Spastics. There have also been two research fellowships in neurosurgery.

Examples of major grants in other fields are £300,000 and £250,000 for halls of residence at the Universities of Glasgow and London respectively, £150,000 for the Institute of Criminology at Cambridge, £65,000 for a chair of metallurgy at Oxford, and £120,000 to the National Playing Fields Association.

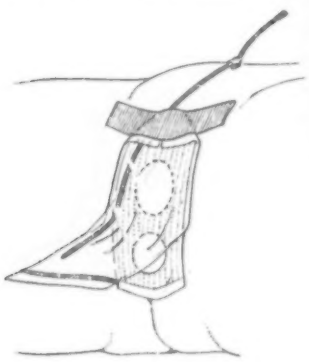
The first volume of an international directory of radioisotopes, containing information on all radioisotopes which are for sale or distribution by the 59 major suppliers in the world, has been published by the International Atomic Energy Agency. The 264-page directory contains tables of radioisotopes, including processed and unprocessed isotope preparations, and solid radiation sources for special applications; the most important physical data, such as half-lives and radiation; some details of preparation and specification of individual preparations; lists of all present suppliers indicating the range of their services, as well as of countries which intend to manufacture isotopes in the near future, and, finally, a guide on the safe handling of radioactive materials. Volume II of the directory, containing complete information on the labelled compounds of ^{14}C, ^{3}H, ^{131}I, ^{32}P, and ^{35}S, will follow shortly. (*International Directory of Radioisotopes—Unprocessed and Processed Radioisotope Preparations and Special Radiation Sources*, 1959. International Atomic Energy Agency, Vienna.)

New Appliances

A SIMPLE URINE COLLECTOR FOR INFANTS

Dr. R. H. WILKINSON and Sister E. M. BALDWIN, of the Metabolic Unit, Hospital for Sick Children, London, W.C.1, write: In 1957 Vesterdal used an adhesive colostomy bag for collecting urine from infants.* This collector has now been modified so that it adheres more satisfactorily, and 24-hour urine collections can be obtained readily from male, female, or pseudohermaphrodite infants. No special bedding is required, and collections can be made in incubators. The method has been used successfully for one year.

Two sizes of polythene bag (12×4 in.—30×10 cm.—and 8×3 in.—20×7.5 cm.), two sizes of zinc oxide plaster (4×4 in.—10×10 cm.—and 4×3 in.—10×7.5 cm.), and a small piece of polythene sheet (2×4 in.—5×10 cm.) are used. The smaller size of bag and plaster are for infants from birth up to the age of 3 months. The plaster is coated on both surfaces with zinc oxide adhesive, over which is a paper covering. Two holes are cut in the plaster—one to surround the vulva (or penis and scrotum) closely, and one to surround the anus leaving a ½-in. (1.3-cm.) margin. The holes are positioned accurately for each infant by inspection. About ½ in. (1.3 cm.) of plaster is left above the opening for the genitalia, and about ½ in. (2 cm.) below the anal opening. On one side of the plaster the paper covering is stripped from the anal end to a line midway between the two openings. A piece of polythene sheet is stuck over the exposed adhesive surface. The paper covering is then completely stripped off and the remainder of the plaster is pressed firmly on to the polythene bag, leaving about 2 in. (5 cm.) of the open end of the bag above the plaster. Thus one surface of the plaster is covered by paper, and the other surface is half covered with the polythene bag and half with the polythene sheet. A hole is cut in the polythene sheet to correspond with the anal opening in the plaster, and a similar hole for the genitalia is cut in the side of the polythene bag adhering to the plaster. The opposite side of the polythene bag is not cut.



Two nurses are needed to fit the appliance. One nurse places the infant on its back, flexes and separates its thighs widely and stretches the skin surrounding the genitalia, perineum, and anus. This decreases the curvatures of the surfaces to which the plaster must adhere. The infant's skin in this area must be clean, dry, and unbroken. The second nurse removes the paper covering from the plaster, places her hand in the open end of the bag, and applies the adhesive surface to the infant, positioning the two openings carefully and pressing the plaster firmly on to the infant's skin. It is most important to ensure good adhesion between the plaster and the perineal skin, as this separates urine from faeces and is the area most disturbed by the passage of hard stools. In difficult cases the skin may be painted with tinct. benzoin. co. (*B.P.*) as an adhesive. The polythene bag adheres to the plaster over the genitalia (see Fig.), but the plaster over half the perineal body and all the anal region is covered by the polythene sheet, which protects the plaster from faeces and can be cleaned easily. Urine

(*Continued at foot of next column*)

(*Continued from preceding column*)

passes through the hole made in the plaster and side wall of the polythene bag down to the closed end of the bag. A catheter is passed to the bottom of the bag. The two corners of the open end of the bag are folded to the centre around the catheter and are secured with adhesive tape. Urine is aspirated from the bag at intervals through the catheter. Using this apparatus, complete 24-hour urine collections may be made for the diagnosis of endocrine, metabolic, fluid, and electrolyte disturbances in infants and young children. It is suitable for surgical patients, provided the operation area is not too close to that covered by the plaster.

We should like to thank Mr. S. Gaillard for his co-operation and Professor A. A. Moncrieff for his help in investigating this collection apparatus.

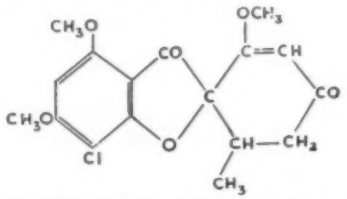
Messrs. Down Bros., 32–4, New Cavendish Street, London, W.1, supply the urine collector (small or large size).

*Vesterdal, J., *Acta paediat. (Uppsala)*, 1957, **46**, 301.

To-day's Drugs

Fulcin (Imperial Chemical Industries).
Grisovin (Glaxo).

These are preparations of griseofulvin, an antibiotic active against fungi. It was isolated in 1939[1] from *Penicillium griseofulvum* and later from other *Penicillium* species.[2] Its chemical formula[3] is as follows:



Animal experiments have shown griseofulvin to have a remarkable antifungal effect in that, when given by mouth, superficial fungus infections of the skin and its appendages may clear up. Its value in the treatment of human infections is now being determined, but preliminary observations show great promise.[4 5]

Side-effects reported so far include occasional headache and dyspepsia, and rashes. The development of leucopenia has been noted in a few cases, and for this reason it would be advisable at present to give it only when careful supervision of the patient is possible and when blood counts can be carried out at weekly intervals.

From the experimental work thus far published it appears that griseofulvin enters the substance of the nail or hair and there exerts an antifungal effect. Superficial infections of the skin may clear up quickly, but presumably nail and hair infections will require a few months' treatment before the infection is eradicated.

The best dosage for treating different diseases has not yet been determined. The manufacturers suggest giving one 250-mg. tablet four times a day (1 g. a day), the dose being increased to 2 g. a day at first in severe cases, with reduction to 1 g. later. The doses for children are lower. Duration of treatment depends on the response of the patient.

N.H.S. basic price: fulcin and grisovin, tabs. 250 mg., 100 for 60s.

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Quarantine Outmoded

SIR,—I agree entirely with the opinion expressed by Sir George Pickering (*Journal*, August 29, p. 305) that small children ought to be exposed to mumps and rubella rather than protected from these diseases while they are at school. In fact, I would go further and say that there should be no routine quarantine for school-child contacts of any of the following common infectious diseases: measles, whooping-cough, mumps, rubella, and chicken-pox. In particular, this should be the practice in all primary and preparatory schools which contain the optimum age-group for catching these common infections, when the disease is likely to be milder, to be less of a nuisance, and to carry much less risk of any serious complication.

School doctors should restrain their natural enthusiasm and not take any active steps to prevent the spread of these common infectious diseases amongst schoolchildren. In my opinion, the infectious diseases regulations at some boarding-schools are far too strict. The instruction about returning to school after exposure to infection during the holidays is unnecessarily rigid, and health certificates might well be abolished, as I doubt very much whether they serve any useful purpose.—I am, etc.,

Public Health Department, City of Oxford. JOHN F. WARIN.

SIR,—Many school doctors do agree that children need not be protected from exposure to the common exanthemata. Quite apart from the desirability of getting these diseases over early, it was shown by Dr. R. E. Smith at Rugby School several years ago that quarantine was an ineffective way of avoiding them. Since in the great majority of epidemics the primary case is not a known contact, the only effect that quarantine can have is to reduce slightly the number of epidemics at the cost of making them bigger.—I am, etc.,

Shrewsbury School. J. C. RYLE.

Mannomustine Therapy

SIR,—Dr. John F. Wilkinson and his colleagues (*Journal*, August 22, p. 208) are to be congratulated on their excellent survey and report on mannomustine ("degranol"), showing its limitations.

In particular, the survival in Hodgkin's disease is poor compared with radiotherapy. In the chemotherapy and hormone clinic attached to the radiotherapy department at the Royal Northern Hospital our impressions were much the same—that is, somewhat disappointing. It is well known that such "cytostatic" remedies have never really cured a malignancy, and, being potent for general damage of the bone marrow, are reserved for those cases in which more radiation is really unsatisfactory as a first measure. The exception is intravenous ^{32}P, which is well known to produce the best results in polycythaemia vera. As both radiotherapy and chemotherapy are under the control of one department, there is no bias either way.

It does appear that there is a strong case for a planned research project to try and elucidate the complex problems of treatment, which are still far from clear in this connexion.—I am, etc.,

Radiotherapy Department, Royal Northern Hospital, London, N.7. ANTHONY GREEN.

Shipyard Eye

SIR,—The story of shipyard eye has recently been described by Dr. E. Jawetz (*Journal*, April 4, p. 873). However, there were omissions in the story, and I will attempt to complete it. The points fall into two groups—first, the historical account of the events leading to the discovery of the aetiological agent, and, secondly, the epidemiology of the disease.

Historical.—As recalled in the story of shipyard eye, only one vial of the Sanders EKC virus remained after the war, and this was identified by Ruchman and Cheever as St. Louis encephalomyelitis virus. This discovery did not fill these scientists with "dismay," as described, but certainly aroused a good deal of curiosity. It opened up the interesting possibility that epidemic keratoconjunctivitis (EKC) and St. Louis encephalitis (SLE) were differing manifestations of the same infection, although what was known of the epidemiology of the two made this seem unlikely. At that time, in 1951, the Encephalitis Investigations Unit of the Communicable Disease Center, United States Public Health Service, was studying the arthropod-borne viral encephalitides, particularly western equine and St. Louis encephalitomyelitis, so that the Unit immediately turned its attention to the Sanders virus.

The first step taken was to investigate an epidemic of EKC in a glaucoma clinic.[1] Next, the specimens of sera collected were tested by Cheever for SLE and EKC antibodies, but no antibodies against these viruses were detected in the sera.[1] Then the one surviving vial of the Sanders EKC was investigated for possible contamination with SLE virus, and it was found not only that the two viruses had been stored in the same deep freeze but that on one occasion, during a power failure and subsequent defrosting over a week-end, the labels had come off many of the vials of viruses and there had been ample opportunity for the viruses to be mislabelled. The view that the SLE virus was not related to the disease was circulated among interested persons in 1951 and published in 1954.[2]

The interest aroused in eye infections in the Encephalitis Investigations Unit led to the recognition in 1951 of a new disease entity, which for convenience was labelled "Greeley disease" after the town in Colorado where it was first noted.[3] This was a disease with pyrexia, pharyngitis, conjunctivitis, and corneal opacities and the resemblance to EKC was clearly noted at the time. In 1951 the adenoviruses had not been discovered and tissue culture was in its infancy, but the sera from the cases in 1951 were saved, so that when Huebner and his colleagues discovered the adenoviruses in 1953 they were able to identify the 1951 Greeley disease as the same as their pharyngo-conjunctival fever and caused by adenovirus type 3.[4] The possibility that EKC was an adenovirus infection was immediately recognized. A search for acute cases of EKC was begun, but the disease in the U.S.A. seemed to have disappeared and the race to isolate the EKC virus was won in California, when a case in the form of an Asian sailor was discovered.[5]

Epidemiology.—It has been clearly established that classical EKC in the U.S.A. is mainly transmitted by the ophthalmologists themselves, but it is also quite clear that this is not the whole story, for there are not enough infective cases in the U.S.A. to maintain the chain of infection indefinitely by this means.[3] The unexplained question was the whereabouts of the virus between the infrequent outbreaks. The sequence of the epidemics in shipyards in the early days of the second world war would suggest a spread from Asia via Hawaii, but that will not account for

the odd small outbreaks that still appear from time to time. The suggestion was put forward at the conference on EKC in San Francisco in 1957 that the EKC virus is a strain of the pharyngo-conjunctival fever virus, arising as a result of the abnormal means of transmission from eye to eye.[6] An epidemic would begin with a patient with the latter attending an eye clinic and resulting in the subsequent serial passage of the virus through a number of eyes. With such passage it would be reasonable to expect the virus to become adapted to growth in corneal tissues and the lesions to increase in severity. Such a concept would explain the sporadic nature of the epidemics and also the fact that in almost all epidemics the first cases are mild and have no corneal opacities.[6] The epidemiology of the disease in the U.S.A. would not be basically different from that in the Orient, as claimed in the "Story of Shipyard Eye." As described there the disease in the Orient associated with adenovirus type 8 is common in children, the symptoms being fever, respiratory symptoms, conjunctivitis, and no opacities; this is, in effect, pharyngo-conjunctivitis and not EKC; 25% to 30% of the population have significant antibody titres to the type 8 virus. The reason why a similar picture is not found in the U.S.A. may lie in the geographical distribution of the virus type 8, which could be basically an Asian virus which spreads to other parts of the world from time to time. However, indigenous EKC viruses in the U.S.A. possibly can arise from the types already present, for type 3 has already been recovered from mild cases of EKC in the U.S.A. and Canada.[7,8] There is no good evidence at present to show that type 8 is the main virus causing EKC in North America, and, indeed, the original isolation in California came from an Asian sailor from a ship.

One difference in transmission may be that, in Asia, flies may play a part. In Ceylon, South India, and Indonesia there are diseases closely resembling EKC, and studies in 1957 in Ceylon revealed no single transmitting agent except for the possibility of flies.[9] At certain times of the year these flies, particularly those sucking the fluids of the eye, are extremely troublesome, and, since they are known to carry the agents of purulent conjunctivitis, it seems likely that they could carry EKC viruses also.

It is suggested that EKC viruses are strains of those causing pharyngo-conjunctival fever selected by repeated passage from eye to eye. In the U.S.A. these strains may arise either from existing indigenous pharyngo-conjunctival infections or be exotic EKC strains imported from the Orient.—I am, etc.,

Dacca, East Pakistan. T. A. COCKBURN.

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Treatment of Pilonidal Sinus

SIR,—Mr. A. J. H. Rains has done a service in bringing to notice (*Journal*, August 15, p. 171) a successful method of primary suture for pilonidal sinus. As he has pointed out, leaving the resulting wound open to heal by second intention is common practice to-day, no doubt because of lack of success with primary suture. Since the difference in time between first and second intention healing may be more than eight weeks, it is not surprising that so called "jeep disease" caused some manpower anxiety during the last war. I have often thought that this loss of time both during the war and since the war and many plastic operations of some magnitude and ingenuity might have been avoided if Oldham's method[1] of primary suture were better known. Using this technique, with certain minor modifications 100% healing by first intention has been obtained in 57 cases in the past twelve years.[2] Registrars and house surgeons have learned the technique easily. It has therefore been puzzling to us to find the literature, year after year, implying that a problem exists.

Perhaps there is space for the briefest general comments on this method. The major factor militating against success is the tendency for the sutured soft parts to assume the position of least tension away from the V-shaped sacral bed. It would seem logical, therefore, to use the same principle as in applying a full-thickness graft to an awkward contour. In other words, firm, even pressure must be maintained by a moulded dressing over the whole area. Oldham's method of applying such an anchor dressing is without rival for this purpose, and, in addition, tension is relieved from the suture line, which other anchor dressings fail to do. The quality of healing often compares favourably with a thyroidectomy scar. Haematoma does not and cannot occur. We do not find injection of dye or hockey-stick deviations of the incision necessary. Comfort is the outstanding feature of this dressing, for which patients and ward sisters will vouch, and no special positioning of the patient is required, who is quickly ambulatory.

Thus, uniformly satisfactory results are obtained by these two rather different techniques. It must be assumed, therefore, that the points in which they differ are probably of less importance than their advocacy suggests, whereas features common to both are likely to be significant. However, if there is any doubt about the most important cause there is none about the most important effect, which is wholly to obliterate dead space and prevent haematoma formation or the collection of exudate.—I am, etc.,

Whipps Cross Hospital, London, E.11. D. L. STEVENSON.

REFERENCES

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2 Stevenson, D. L., *Postgrad. med. J.*, 1948, **24**, 470.

SIR,—In his article on pilonidal sinus (*Journal*, August 15, p. 171) it is a pity that Mr. A. J. H. Rains did not refer to exteriorization of the sinus track and its ramifications as a method of treatment.[1] Its advantages are that it is a much more simple procedure to perform than excision and primary suture: moreover, if the floor of the sinus is not curetted but cleaned gently with a dry swab, islands of squamous epithelium are not removed and thus healing is very rapid and uneventful. The patient is usually discharged from hospital within ten days and returns to work shortly afterwards.

While excision and primary closure is attractive as a method of treating pilonidal sinus at first sight, it has the following serious disadvantages: (1) It is time-consuming and the greatest possible care must be taken to avoid haematoma formation, which if it occurs is almost always followed by secondary infection and breakdown of the wound, necessitating a prolonged stay in hospital. (2) Soft tissues are removed from an area where there is little tissue to spare and where dead space is very liable to occur. (3) It cannot be entrusted with safety to the inexperienced surgeon if consistently good results are to be obtained.

The operation of total excision of the sinus, allowing the cavity to granulate, is antiquated and has no place

in the modern treatment of pilonidal sinus, except possibly in the treatment of chronic recurrent pilonidal sinus, when primary total excision with immediate split-skin grafting may be the treatment of choice.—I am, etc.,

P. G. COLLINS.

Sheffield, 6.

REFERENCE

[4] Patey, D. H., in *Operative Surgery*, 1958, Progress Volume, edited by C. Rob and R. Smith, p. 60. Butterworth. London.

Physic and Metaphysic

SIR,—It is naturally gratifying for a layman to find his book on a medical subject reviewed at some length in the *Journal*; and I must thank Dr. William Sargant (*Journal*, August 15, p. 177) for the courteous restraint with which he criticized opinions so different from his own. But may I comment on the central point he makes when he argues that, "despite the part *obviously* played by stresses of various kinds in bringing on attacks of tuberculosis, this killing disease has been dealt with far more effectively with the discovery of I.N.A. and P.A.S."?

I have italicized "obviously" because, though the part stress plays may be obvious to a member of the medical profession, it certainly is not to the public. Preparing the book, I was anxious to find how far friends, colleagues, and acquaintances were aware of the research of Wittkower, Kissen, and others into the links between emotional stress and tuberculosis. I encountered nobody outside the profession who had ever heard of it. Most people I asked were under the impression that the idea of tuberculosis being in any sense a nervous disorder was an exploded nineteenth-century myth, which was one reason why the book was written.

It is true, of course, that the existence of a stress component in an illness need not determine the nature of the cure. The fact that the cause of, say, a road accident is "psychological," in the sense that the victim was too preoccupied with his worries to look where he was walking, does not mean that the ambulance should bring him to an analyst rather than to a casualty ward; in many diseases, as Dr. Sargant says, drugs can by-pass stress. But it was not my object to deny the efficacy of drugs in treatment. I was simply arguing that if emotional stress is a significant component in more diseases than is commonly realized (and this, I submit, has now been adequately confirmed by research), then there is renewed hope that the family doctor, provided he has the necessary sympathy, will be able to detect the symptoms *before* illness strikes. My book is indeed special pleading; but it is on behalf of the family doctor—not of some vague abstraction called psychosomatic medicine.—I am, etc.,

BRIAN INGLIS,
Editor, *The Spectator*.

London, W.C.1.

Riedel's Thyroiditis

SIR,—I wish to congratulate Drs. A. Graham and I. C. Gilliland on their excellent account of Riedel's thyroiditis (*Journal*, August 22, p. 225). I should like, however, to question a rather minor point. The authors state the diagnosis can only be made on histological grounds which ". . . demands evidence of replacement of thyroid tissue by dense solid fibrous tissue. . . ."

Nevertheless, Riedel himself stated: "If you look at the microscopic preparations you will find collections of round cells interspersed among normal thyroid tissue whereby the latter has been more or less destroyed. By just looking at the preparations one has no idea of how hard the tumour is; one expects solid fibrous tissue to constitute the tumour, but, as has already been said, one finds only embedded round cells." It is as well to remember that Riedel's three cases all died under mysterious circumstances without necropsy some years after their illness. In our present state of ignorance it may be as well to regard Riedel's illness as a clinical syndrome and not a pathological entity.—I am, etc.,

ANGUS E. STUART.

Edinburgh, 1.

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[3] —— *Münch. med. Wschr.*, 1910, **57**, 1946.

High Pyrexia Due to Sulphadimidine

SIR,—Two children, aged about 8 years, were being treated for acute nephritis and acute rheumatic fever respectively, following an epidemic of tonsillitis. Both were improving in condition following an initial course of penicillin and standard treatment for their disease, and they were being given 0.5 g. of sulphadimidine twice a day. Both became febrile, with temperatures over 103° F. (39.4° C.) daily, without other signs of relapse of their disease. No alternative cause for the pyrexia was found.

The child with nephritis was showing progressively less albumin and fewer cells in her urine, despite the pyrexia, which lasted for a week. She had a rash of very small papules like exaggerated "goose-flesh," which gradually faded after sulphadimidine was ceased. She became afebrile within 48 hours of the cessation of this drug. After three more days she was given one more 0.5-g. tablet, and within an hour she became prostrate with a severe rigor. Within 24 hours her condition was stable again.

The second patient, with rheumatic fever, was asymptomatic on salicylate therapy, when his temperature rose again. The temperature also fell with the cessation of sulphadimidine. He showed a similar response to 0.25 g. of sulphadimidine after being afebrile for two days. The blood film of the first child appeared normal during her period of pyrexia.—I am, etc.,

D. R. LITHGOW.

Indian Hospital,
Namosau, Fiji.

Listerial Meningitis in Infants

SIR,—May we beg the courtesy of your columns to give a follow-up report on the two cases of listerial meningitis described by us in your *Journal* of July 27, 1957 (p. 188)?

Case 1, Baby Ross aged 3 months at the time of his illness, has remained well since discharge from hospital in May, 1956. A recent check has revealed no signs of hydrocephalus and the child is clinically normal. The case was not a severe one, though well-marked meningitis was shown by the presence in a slightly turbid C.S.F. of numerous polymorphs and a moderate number of *Listeria monocytogenes* (type 4b).

Case 2, Baby Fraser, developed meningitis in May, 1956, aged 10 days. Numerous polymorphs and *Listeria monocytogenes* (type 2) were present in the (cloudy) C.S.F. A generalized convulsion occurred shortly after admission and occasional twitching thereafter for 33 days. Although clinically normal on discharge (June 16, 1956), hydrocephalus ensued gradually. A ventriculogram in March, 1957 (performed in the Royal Infirmary, Edinburgh), showed complete obstruction of the aqueduct. Attempts to by-pass

the obstruction by ventriculo-cisternotomy and theco-peritoneal anastomosis (April 11, 1957), and ventriculo-peritoneal anastomosis (June, 1957), had little effect, and gross dementia and physical under-development occurred. The child died on April 4, 1959, of terminal haemolytic streptococcal septicaemia.

The initial treatment given to the two cases was as follows:

Case 1.—Penicillin 1 mega unit intramuscularly, followed by 250,000 units 6-hourly, continued for 6 days. Sulphadiazine, 0.5 g. 6-hourly (17 days) and chloramphenicol, 125 mg. 6-hourly (10 days) were also given. In view of a slightly fluctuating temperature, chlortetracycline, 15 mg. 6-hourly, was given on the 16th day for 6 days. The organism was sensitive *in vitro* to all the drugs used.

Case 2.—On admission, streptomycin 50 mg. b.d., intramuscularly, and sulphadiazine 0.5 g. followed by 0.25 g. 6-hourly by mouth (18 days) was given. After the first day, streptomycin was replaced by chloramphenicol 125 mg. 6-hourly for 12 days. On the 19th day after admission terramycin 50 mg. followed by 25 mg. 6-hourly was given for 18 days. The listeria strain isolated was sensitive *in vitro* to all the drugs used.

In both cases, therefore, prolonged antibiotic treatment was given. Penicillin was not used in Case 2, which has now died, but the other drugs used have been effective in the limited experience of other workers so far. Seeliger and Cherry[1] recommend a combination of sulphonamide, penicillin, and tetracycline provided treatment is started early and adequate drug levels maintained for a sufficient period.—We are, etc.,

P. N. EDMUNDS.
D. N. NICHOLSON.
D. M. DOUGLAS.

Bacteriological Unit,
Astley Ainslie Hospital,
Edinburgh.

REFERENCE

[1] Seeliger, H. P. R., and Cherry, W. B., *Human Listeriosis*, 1957. U.S. Dept. Hlth., Education and Welfare, Atlanta, Georgia.

First-aid Splints

SIR,—Country practitioners who frequently lose their splints at the hospitals to which they send their casualties might be pleased to learn of a cheap and useful first-aid splint for fractures of the leg. Two 3 ft. (0.9 m.) garden canes inserted into a lady's nylon stocking provide comfortable support for an adult. A bandage or handkerchief passed under the upper free ends of the canes and tied over the leg supports the upper end, and the lower end can be similarly supported by making holes in the stocking and tying a bandage over the ankles. Padding will prevent pressure of the canes on knee and ankle, and the whole can be stabilized by bandaging.

For fractures of the wrist and forearm use can be made of the "divisions" in wine (or spirit) dozen-cartons. If these are pushed into a nylon stocking and then opened out a very comfortable cradle is formed, and this can easily be fixed by a bandage. Incidentally, the room in one's car taken up by the canes, etc., is much less than by an orthodox splint.—I am, etc.,

Faringdon, Berks. GRAHAM STENHOUSE.

The Occasional Obstetrician

SIR,—Despite the many words of wisdom about domiciliary obstetrics expressed in your columns (*Journal*, August 1, p. 104, and August 22, p. 245), there is one aspect I have not seen mentioned. That is the inestimable value that the confidence of the woman in labour in her own doctor has on the course of labour. I feel that one ounce of this confidence is worth more than a pound of experience by an impersonal "G.P. Obstetrician" who may be quite unknown to the patient.

Of course, this is one of those intangibles of life that cannot be assessed statistically by consultant committees. The trouble is that every few weeks some new committee advises on how we should do our obstetrics, or how we should prescribe, or how we should make our deputizing arrangements, or how much we should be paid, etc., etc. The danger is that lofty committees will one day descend from their Sinai and produce a medical decalogue with its "Thou shalts" and "Thou shalt nots"—on penalty of this or that. Our personal and professional freedom, much of which we have already sacrificed, will then surely be doomed.—I am, etc.,

London, N.10. B. W. PERLOW.

When to Tie the Cord

SIR,—A local midwife has recently taught me some pearls of wisdom. One concerns "stripping the cord." I have done it perhaps more gingerly than she for fear of over-distending the systemic venous circuit, probably over-cautiously. The technique is to milk the extruded section of cord from birth canal to baby with finger and thumb as soon as the neonatal lungs inflate. My impression is that this speeds cessation of cord pulsation and allows visual evidence of the rate of blood return from the placenta, as the vein walls are quite translucent and even a drop of blood is easily picked out as a blue shadow. Should placental return flow be obvious the stripping can be repeated. The marked reduction in size of the cord upon stripping, frequently to a third of its original calibre, attests the amount of blood saved.

Since these observations I have noted that an unstripped cord of its own accord rapidly constricts to about half its original calibre, usually starting from the umbilicus, by the time pulsation is noticeably lessened. Some obstetrician with stop-watch and callipers might be able to correct me.—I am, etc.,

Rockhampton, Queensland. DOUGLAS EVERINGHAM.

Living in Caravans

SIR,—Your annotation (*Journal*, August 29, p. 296) draws attention to a number of problems arising from residential caravanning. No doubt the answers to some of them will be cleared when the Minister has announced the result of his study of the report by Sir Arton Wilson which is now in his hands. I point out that several other difficulties are the kind of thing likely to arise wherever demand exceeds supply and are not evils inherent in residential caravanning. No legislation, for example, will stamp out the practice of what you call "place money" any more than it has been able to stamp out the payment of premiums for houses and flats.

You refer to caravans being placed on unlicensed sites. No doubt these sites have no licence under the Public Health Act, but the word "licence" is loosely used and "unlicensed" generally means "without planning permission." While a site may not be used for more than 42 consecutive days or 60 days in any 12 months without a public health licence, the limit under the planning legislation is 28 days from the day when development begins. It is not correct that planning permission can be refused only on the ground of damage to amenities. Local planning authorities

may refuse it for any reason which is consistent with the aims of the 1947 Act—for example, because it does not conform to the development plan or because it is not in their opinion an appropriate use of the land.—I am, etc.,

W. M. WHITEMAN,
Editor, *The Caravan*.

London, W.C.1.

Iproniazid in Depressive Syndrome

SIR,—When drug therapy is really effective it is generally apparent to both doctor and patient alike, and this does seem to be the case with the use of iproniazid in the group of "atypical" depressions we have described (*Journal*, June 13, p. 1491). Dr. P. H. Gwynne, however, feels (*Journal*, August 22, p. 241) that this particular group is "most susceptible to placebo suggestion." We do not know what his experimental evidence is for this statement, because we have, on the contrary, found these particular patients to be very poor placebo reactors indeed, both experimentally and because so many other treatments have failed to help them in the past.

Since completing our paper, we have, however, carried out a "blind" trial on 28 of these atypical depressions, comparing iproniazid with an inert placebo (calcium lactate). Each substance was given for 4 weeks, and the results are shown below. The differences are, of course, highly significant.

	Improvement		
	None	Slight	Marked
Iproniazid ..	6	3	19
Placebo	20	7	1

Dr. Gwynne may argue that, as the trial was not a "double" blind, these results can be in part due to our own enthusiasm. The best thing to do would be for Dr. Gwynne to try out the drug for himself in this particular group. He writes, however, that the "extreme toxicity of iproniazid cannot be ignored," and that "a patient is better off with an atypical depression and an intact liver than an intact personality with acute hepatic failure." By this statement he seems to be unaware of the amount of suffering and disability that can be caused by these atypical depressions, and in our view he is exaggerating the risks involved. Iproniazid can occasionally be a very toxic drug, but justifiable risks do sometimes have to be taken in psychiatry, as in all other branches of medicine. Actually in this department we have only had 2 non-fatal cases of jaundice in over 1,000 patients treated with iproniazid over the past 2 years. This can hardly be called "extreme toxicity" and a large number of patients have been helped. However, we hope that even this hepatic risk will soon disappear, since the newer amine oxidase inhibitors we are now testing out are proving to be both therapeutically effective and, so far, non-toxic to the liver.

We are quite aware of both the advantages and disadvantages of double blind trials. But we doubt whether, in fact, we should have found out this particular group and its specific response to iproniazid if we had used such methods in our investigation, instead of more clinical ones in the appraisal of this drug.—We are, etc.,

E. D. WEST.
P. J. DALLY.

St. Thomas's Hospital,
London, S.E.1.

Drug Addicts

SIR,—It occurs to me to bring to your attention a method by which drug addicts are able to obtain drugs even when under treatment. They will go to any doctor's surgery and obtain a prescription for drugs. The most persistent of them can tour quite a number of doctors. Sometimes they are able to persuade friends or relatives or other patients to do this for them. Some people remain on the fringe of addiction and do not see anything wrong in obtaining drugs by this method for a patient who is suicidal, but without the initiative to obtain drugs for himself. I have also had reason to suspect that this method of obtaining drugs was being used by patients and ex-patients to join in drug trafficking.

I feel that it must be often impossible for a doctor to evaluate appeals for help presented by patients who are strangers to him. I hesitate to add to the burden of practitioners, but it should not be beyond our ingenuity to avoid promoting patients' suffering in this way. The good name of the profession also suffers. It may be, for example, that there could be an understanding amongst general practitioners not to supply dangerous drugs to someone who is not their patient without being presented with a letter or prescription from their usual doctor, and this would be within the spirit of the Dangerous Drugs Act. It would have to be done on a national scale, since these patients wander far and wide in their attempts to escape the implications of their illness.

While on this subject, such patients often belong to the medical and ancillary professions. It seems to be a very common practice to enable them to move to another district easily by supplying them with glowing testimonials, presumably with the intention of helping them. I would suggest that this has the opposite effect, and that the best that could be done for them would be to ensure that they face their difficulty and have treatment at the earliest possible point.—I am, etc.,

H. A. ANDERSON.

Ilford, Essex.

Inoculation Recording by Tattooing

SIR,—The only inoculation requiring a readily available permanent record is tetanus toxoid. Tattooing offers the most satisfactory solution to the record problem, as the alternatives (cards, disks, etc.) may be lost, destroyed, or simply left at home. To be practical the technique must be simple, and the tattoo easily found but sufficiently insignificant to be aesthetically acceptable. Mr. Norman Lake (*Journal*, August 8, p. 141) has designed a new instrument for tattooing, but I found experimentally some three years ago that the Heaf gun gave very good results. I used it to tattoo through a drop of sterilized Indian ink, the technique being the same as that for a Mantoux test. The procedure was simple to perform and quite painless. A clear ring of five dots (one of the needle points having been broken off previously), unobtrusive but easily recognized, was produced. Mr. Lake logically suggests a T-shaped design, although the actual shape is immaterial provided it is universally accepted and tattooed at an agreed site. As the Heaf gun is already available the design produced by it might prove acceptable.

The site is largely determined by aesthetic considerations. I think the most acceptable is just above or below the iliac crest. I usually ask parents at the time of their child's inoculation whether they would

object to this type of tattoo. I have had very few objectors when the need for tattooing in the case of tetanus was explained to them.—I am, etc.,

Ixworth, Suffolk. ALAN J. ROWE.

Cracked Foreskin

SIR,—I was interested to read Dr. Kenneth Bhagan's letter (*Journal*, April 18, p. 1046) which reported 11 male patients with cracked foreskin and glycosuria.

In the eight months I have been practising here we have seen three middle-aged male patients who presented at this clinic (a group practice of three) with balanitis and were found to have glycosuria on routine urine test. Two had a diabetic glucose tolerance curve. The third man did not return for investigation and treatment.

Of the other two, one recovered from his balanitis when his diabetes was stabilized (he is now stabilized on diet alone). The other patient refused to co-operate with dietary measures and had to be stabilized in hospital. Dr. John Fitzwater stabilized him in hospital in Brisbane. On discharge, this patient's balanitis was improving. He has not returned for follow-up.—I am, etc.,

Southport, Queensland. FRANK L. JOHNSON.

Anaesthesia for Bronchoscopy

SIR,—The letter by Mr. Michael Bates on anaesthesia for bronchoscopy (*Journal*, August 15, p. 191) is very interesting, and I would like to support his contention that local analgesia has advantages, especially in older people. For many years the surgeons for whom I gave anaesthetics expected me to use analgesia, and now for less than two years we have mainly used general anaesthesia. I see several noticeable differences between the two techniques.

Firstly, under anaesthesia the patient is oblivious to what happens and there is little for him to complain about afterwards. One must admit that this is not always true of analgesia, although for several reasons the number of partial failures with this method could be reduced. On the other hand, while I have never heard of a death associated with analgesia, I have seen and heard of several dying either under anaesthesia or within 36 hours of the procedure. As Mr. Bates mentions, coughing, which can be very severe and prolonged, is almost a constant feature after bronchoscopy under anaesthesia, even though the full local technique has been used in addition. This coughing is rarely seen when analgesia has been used for bronchoscopy and I do not know why it occurs after anaesthesia. The time factor is very different in each case. Some two to three minutes will suffice to produce analgesia, and once the bronchoscope has been passed the anaesthetist can proceed to the next patient. A general anaesthetic can be very worrying in the elderly with poor pulmonary function, and they must be carefully watched in the immediate post-operative period. Recently I was 4½ hours with such a patient when spontaneous respiration did not return after the administration of 70 mg. succinylcholine.

The technique which we copy is not new, but is, I think, simpler than that quoted by Mr. Bates. Adequate sedation, correctly timed, and an amethocaine hydrochloride lozenge, which has in fact been sucked and not just allowed to lie undissolved in the mouth, are essential. Spraying the mouth and pharynx with an analgesic before bronchoscopy was no substitute for the lozenge. Analgesia of the bronchial tree is obtained by two injections through the crico-thyroid membrane. The first, of 1–1.5 ml. lignocaine hydrochloride, is given with the patient in the horizontal position, and will render insensitive the vocal cords and have some effect on most of the bronchial tree. Slight coughing usually follows and saliva stained by the injected solution is often seen, so proving that it has passed the vocal cords. The small dose reaching the bronchial tree does much towards reducing the coughing which would otherwise follow the second and larger injection. This is given with the patient sitting up; the neck is slightly extended and the nurse on the patient's left supports the occiput with her right hand. When the needle has been correctly positioned the patient is asked to lean to the left and is helped and supported by the nurse. Some 2.5 ml. is then injected, making a total of 4 ml. lignocaine. The object of this second injection is to reach the basal orifices, and the lateral tilt directs some into the lingula. If only one injection is given distressing coughing can occur and not infrequently the basal orifices are inadequately covered. Giving the double injection causes little discomfort and the results are better.

It must always be borne in mind that unless the operation is gentle no form of surgery can be successful under analgesia, and in these circumstances it should not be used. Trainee bronchoscopists should be included in this group until they have reached the high standard set by thoracic units. I suggest that both techniques should be used. General anaesthesia is probably better for fit people up to the age of about 50 years and those with a full complement of teeth, particularly if the mouth is small; the very apprehensive patient should be asleep. Analgesia should be used for most seriously ill patients and those with poor pulmonary function; all of them should have the eyes covered before the bronchoscope is passed. If I were the patient I should choose my surgeon and then insist on analgesia.—I am, etc.,

Southsea. H. B. C. SANDIFORD.

Diabetes in the Tropics

SIR,—It seems to me that the only way to prove or disprove a hypothesis is to design and execute a suitable series of experiments. Dr. A. Paton (*Journal*, July 4, p. 20) refers us instead to three interesting papers[1 2 3] quoting a number of cases where diabetes seems to wane temporarily or in some instances apparently permanently. These three papers all suggest that the liberal use of insulin in the early stage of diabetes may lead to a more rapid, more complete, and perhaps longer-lasting normalization of carbohydrate tolerance than any other method. Clinical and experimental evidence produced recently[4] is at variance with this recommendation.

We seem to understand little but the most urgent uses of insulin such as its use in the prevention and treatment of diabetic ketosis. The classical *symptoms* of diabetes are treated by a trial-and-error method using arbitrary amounts of insulin. We thus diminish glycosuria and reduce the occasional blood sugar to a figure which satisfies our therapeutic conscience. At the same time, juggling with the many delayed insulins allows us to dogmatize on their various merits, tending to forget that their absorption does not, as in the case of islet cell insulin, depend upon the blood sugar concentration of the surrounding medium, but solely upon the characteristics of the combination of insulin with a salt or ion.

Many physicians believe that a "well-controlled" diabetic will do better and have fewer complications than a "badly controlled diabetic."[5] Others can't help wondering whether it was the control that was bad or the disease itself, in the group that had most complications. In other words, had they a type of disease not amenable to good control, and at the same time liable to complications? Finally, views differ as to the relative importance of good biochemical control in the middle-aged and elderly diabetics once symptomatology is brought under control. Beyond all this we have not learnt much which might improve upon our present therapeutic use of insulin. After thirty-eight years one might expect a little more information, and certainly willingness, co-operation, and facilities to obtain this information.

My initial, perhaps somewhat intrepid note (*Journal*, June 6, p. 1473) expressed the view that, unless controlled epidemiological and biochemical studies are applied to our diabetic patient population in several large clinics in each country, your readers will continue to have to listen to sterile arguments in your correspondence columns.—I am, etc.,

Johns Hopkins Hospital,
Baltimore, 5, Md. FREDERICK WOLFF.

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[1] Harwood, R., *New Engl. J. Med.*, 1957, **257**, 257.
[2] Goadby, H. K., *Acta med. scand.*, 1943, **115**, 247.
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[4] Volk, B. W., Lazarus, S. S., *Amer. J. med. Sci.*, 1959, **237**, 1.
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Subject in Search of a Name

SIR,—Might I suggest that ecological medicine is a suitable name to include public health, epidemiology, social medicine, industrial medicine, population pathology, and group medicine? All these subjects are concerned with the study of man and his relationships with his environment, whether this is biological, physical, or social. The term human ecology is too wide, as there is much in human relationships that is not medical. To put it in another way, ecological medicine means medicine applied to the study of human relationships. Other branches of medicine might claim to be *syncritic* (to adopt Dr. A. M. McFarlan's term, *Journal*, July 4, p. 21), but all branches of medicine for which Professor L. J. Witts (*Journal*, May 2, p. 1190) is anxious to find a name are concerned with human relationships.—I am, etc.,

Department of Social
Medicine and Public Health,
University of Malaya. T. A. LLOYD DAVIES.

Anglo-German Medical Society

SIR,—With regard to the letter by Drs. W. Walker and E. Kawerau (*Journal*, August 29, p. 307), do you think that the time is ripe for founding such a society, with the horrors perpetrated by members of the German medical profession (and many other Germans) still in our minds?—I am, etc.,

London, N.W.4. F. DANNHEISSER.

Leeds General Infirmary

SIR,—I am working on the history of the General Infirmary at Leeds. I would be most grateful for information about any relevant letters, documents, portraits, etc. If any such were lent to me they would be copied and returned without delay and due acknowledgment to the owner would be made in the text.—I am etc.,

Leeds, 1. S. T. ANNING.

Obituary

Sir WALTER HAWARD, O.B.E., M.B., B.S.

Sir Walter Haward, formerly director-general of medical services of the Ministry of Pensions, died at Queen Mary's Hospital, Roehampton, on September 2. He was 77 years of age.

Walter Haward was born on January 23, 1882. His early years as a medical student were spent at Durham University, and he went on to St. Thomas's Hospital for his clinical training. He took the London Conjoint diploma in 1904, obtaining the Durham degrees of M.B., B.S., with honours, in the same year. After qualification he held the appointments of assistant house-physician and house-physician at St. Thomas's Hospital, and from 1905 to 1915 he was in private practice. He served in the R.A.M.C. during the first world war, attaining the rank of major, and was officer in charge of the medical division of the 36th General Hospital attached to the Serbian Army, and, later, of the 28th General Hospital of the Army in Salonika. In this notoriously unhealthy theatre of war he contracted dysentery, which was to give him some trouble in later years. He was mentioned in dispatches, and in 1918 the Order of St. Sava (fourth class) was conferred upon him by the King of Serbia.

[*Walter Stoneman*

After the war Haward joined the staff of the Ministry of Pensions as deputy commissioner of medical services. He progressed to principal medical officer in 1925 and to assistant director of medical services in 1938, becoming director-general in 1942. He retired in 1947. Appointed O.B.E. in 1938, he was knighted in 1944. From 1947 to 1950 he was an Honorary Physician to the King. In 1905 he married Miss Louisa A. Mann, and she survives him. There were five children of the marriage, one son and four daughters.

F. T. R. writes: His old colleagues in the Ministry of Pensions will have heard of the death of Sir Walter Haward with much sorrow. This sad news will evoke in their minds many memories of his genial and kindly personality, his unfailing courtesy, which had something of an old-world touch about it, and the warmth and sincerity of his friendship. Among the many likable qualities that endeared him to his staff, perhaps not the least was the generous way in which he always acknowledged the support they gave him. He was a most approachable man, and, however busy, would always find time to see any member of his staff who wished to discuss a difficulty, official or otherwise, with him.

When he joined the medical staff of the Ministry of Pensions in 1919 Haward was concerned with the pensions side of the Ministry's work. He had made a close study of the many problems relating to title to pension and the assessment of the degree of disablement resulting from war service. The organization and guidance of the large number of medical boards that had been set up in all parts of the country was his responsibility and one which he discharged with outstanding success.

Haward was appointed director-general in 1942, when invalidings from the Services were increasing rapidly. The provision of treatment for war-disabled pensioners, at an ever-expanding rate, was to be his main concern during his five years as head of the Ministry's medical services. The duties of his office in the war years made unrelenting demands upon his time and energy, but he could never be

persuaded to slacken the pace or spare himself in any way. A wise and able administrator, he enjoyed throughout his career the confidence of his colleagues, both lay and medical. Our sympathy goes out to the devoted family circle who mourn his loss. That his son had followed him into the medical profession gave him great satisfaction. Those of us who were his contemporaries in the old Ministry will hold his memory in affection and esteem.

H. W. BARNES, M.B., B.Chir., D.P.H.

Dr. H. W. Barnes, who was medical officer of health for Camberwell for 34 years, died at his home at Frinton-on-Sea, Essex, on August 31, three days before his 72nd birthday, after a long period of ill-health.

Howell Wood Barnes was born in Barbados, British West Indies, on September 3, 1887. From Jesus College, Cambridge, where he graduated B.A. in the Natural Sciences Tripos, he went on to St. Bartholomew's Hospital, qualifying M.R.C.S., L.R.C.P. in 1911. Two years later he graduated M.B., B.Chir., and in 1914 he took the Cambridge D.P.H. During the first world war he was in the R.A.M.C. from 1915 to 1919, and saw service on the western front. After having held public health appointments at Lincoln, Exeter, and Yeovil, and as a temporary medical officer with the old Local Government Board, he became medical officer of health for Camberwell in 1921, and remained there until his retirement in 1954.

Barnes was Camberwell's third medical officer of health, following Dr. Francis Stevens and Dr. J. S. Bristowe, F.R.S. Between them they covered a period of a hundred years of preventive medical practice, from 1855, when, after the passing of the Metropolis Local Management Act, the first medical officers of health were appointed in London, until 1954. When he assumed office shortly after the end of the first world war, Barnes had already worked for a time with Dr. Stevens, and in the inevitable period of change which followed he blended the lessons of the past with the needs of the present. This was a principle he applied successfully, and unassumingly, throughout his public-health career.

Thanks to his foresight and enthusiasm, Camberwell became one of the first boroughs to embark on an intensive diphtheria immunization campaign; he was always a staunch advocate of wider and better health educational schemes. A closer linkage between preventive and curative medicine was one of his ideals, and the success he achieved in this direction was in no small measure the result of his friendly disposition and delightful manner. Under his guidance the personal health services of the borough became comprehensive and efficient and he was justifiably proud of the organization he handed over to the London County Council in 1948, though he never ceased to regret the necessity for having to do so. When the last war came he devoted himself with characteristic efficiency to civil defence work; he also became a prominent figure on the local medical committee.

Barnes never sought the limelight, and on the surface he did not take a very active part in the work of his professional organizations, but he was a staunch supporter both of the Society of Medical Officers of Health (he joined in 1919 and was elected a life member) and of the British Medical Association; neither did he contribute to any extent to medical literature, other than in his informative and progressive annual reports as medical officer of health. The contribution he made to public health in the metropolis was none the less very considerable, and many of the younger generation will remember his thoughtful appraisal of a problem and his wise counsel.

He was a keen sportsman, and in his younger days at Cambridge showed great prowess as a cricketer. He is still remembered for his big hitting in the Camberwell municipal officers' team, which resulted in many lost balls. In his later years, despite a good deal of ill-health, of which he made light, he was an enthusiastic golfer.

The memory of his genial personality, friendliness, and quiet efficiency will long remain with his colleagues in Camberwell, within and without the town hall; with the public whom he served so well; and with a host of old friends in the public health world outside. He leaves a widow and two married daughters, to whom we extend our deep sympathy.—H. D. C.

JAMES SHARPE, M.B., F.R.F.P.S., D.P.H.

Dr. James Sharpe, who was in general practice in Sheffield for nineteen years, died on August 5. He was 62 years of age.

Born at Closeburn, Dumfries, on April 22, 1897, James Sharpe was educated at the Wallace Hall Academy. He received his medical training at Glasgow, where he obtained the Scottish triple qualification in 1925. Taking the Glasgow degrees of M.B., Ch.B. in the following year, he went on to acquire the D.P.H. of the Scottish Royal Corporations in 1928, the Fellowship of the Royal Faculty of Physicians and Surgeons of Glasgow in 1930, and the Leeds Diploma in Public Administration in 1939. In his early postgraduate years he held appointments at the Royal Mental Hospital, Gartnavel, Dykebar Asylum, Heathfield Hospital, Ayr, and at Wishaw Sanatorium. He then became deputy medical superintendent of the County Hospital, Motherwell, and clinical assistant in Dr. James Carslaw's wards at the Western Infirmary, Glasgow. While attending the Western Infirmary he was appointed an examiner in venereal diseases of candidates for the D.P.H. and the Fellowship of the Royal Faculty of Physicians and Surgeons.

In 1934 he was appointed deputy medical officer of health for Leeds and honorary demonstrator in public health at Leeds University. Six years later he took up general practice in Sheffield, where he took an active part in medical affairs. He represented his Division at several Annual Representative Meetings of the B.M.A., and for a year or two he served on the Public Health and Private Practice Committees. In 1955–6 he was chairman of the Sheffield Division.

A colleague writes: James Sharpe was a man who possessed abundant energy. In addition to attending faithfully to his practice he had many other duties. He was medical officer of the rehabilitation and training centre and of the mines mechanization and National Coal Board centre, both at Sheffield. He was also a medical referee to the Ministry of Labour and National Service, a member of the interviewing committee of the disablement and resettlement service, and deputy police surgeon to Sheffield. When the National Health Service came into being in 1948 he was the first chairman of the local medical committee. James was a very kindly man with a "pawky" sense of humour which endeared him to all. He enjoyed life to the full, and was the perfect host. He was an enthusiastic supporter of the Sheffield Caledonian Society, of which he was president in 1950–1. Despite a major operation nine years ago and a severe attack of coronary thrombosis six years ago, he returned to his numerous duties with seemingly renewed vigour. He will be sadly missed by his many patients, friends, and colleagues. He leaves a widow and one son.

Dr. E. ASHWORTH UNDERWOOD writes: I was a close friend of "Jimmie" Sharpe over a period of nearly 40 years. We first met in a laboratory at Glasgow University in 1921; we were much associated in connexion with the University Dumfries and Galloway Society, of which he was secretary when I was president; he was deputy medical superintendent of the County of Lanark Fever Hospital at Motherwell when I was assistant medical officer of health for that county; he succeeded me as deputy medical officer of health of the City of Leeds in 1934; and during the later years, while we were each following our individual paths, he in Sheffield and I in London, we met as often as possible and recaptured at these meetings—I venture to hope—something of our youthful enthusiasms. (Our correspondence was sporadic and not always completely rewarding; for, while my

writing may be the subject of severe stricture, Jimmie wrote the most microscopic of hands which must have been a terror not only to examiners but to all who had subsequently to dispense his prescriptions.)

Perhaps Jimmie's most outstanding characteristic was his intense interest in humanity. He was a born "doctor." On leaving Wallace Hall Academy he joined the R.A.M.C. and served in Mesopotamia. After a rather late demobilization he was for a short period assistant to a pharmaceutical chemist in Dumfriesshire, and when he commenced his medical studies at Glasgow he already had some knowledge of therapeutics. It was this preoccupation with human nature which led to his early interest in mental diseases, and to several resident posts in mental asylums in the West of Scotland. At that period I thought he would become an alienist. But his considerable experience of infectious diseases led to an interest in V.D., and in November, 1929, he succeeded Dr. Robert Forgan as executive medical officer of the Lanarkshire Joint Committee on V.D., a post which he held with distinction until he went to Leeds in October, 1934. Despite his great experience in public health—he was president of the Yorkshire Branch of the Society of Medical Officers of Health in 1940—I feel that his decision early in the war to settle in general practice was probably right. Of his work in rehabilitation and industrial medicine in Sheffield others will speak; but probably none of his hundreds of grateful patients in that city will ever have the opportunity to write of what they owed to him.

Very few medical men will realize that for the last 25 years of his life Jimmie was more than in theory physically incapacitated. In 1934 he had one kidney removed for calculus. Fourteen years later he had to have a nephrotomy on the other kidney for the same condition. Despite an attack of coronary thrombosis he carried on with his vitality seemingly little impaired. As a man, as a doctor, and as a friend he will be difficult to replace.

LASAR DUNNER, M.D.

Dr. Lasar Dunner, honorary physician in charge of the industrial chest diseases clinic, Hull, died suddenly on June 6 while on holiday in Germany, eight days before his 74th birthday.

Lasar Dunner was born at Cologne on June 14, 1885, and was educated at Wurzburg, Munich, and Berlin, graduating M.D. from Berlin University in 1912. Thenceforward his main interest was in the study and treatment of pulmonary diseases, and before the Nazi regime forced him to leave Germany he had held the appointments of chief physician in the department of respiratory diseases of the Jewish Hospital, Berlin, and chief physician and medical director of the Buch-West Hospital, also in Berlin.

R. H. writes: Dr. Lasar Dunner had already attained a high professional reputation in his own and other European countries before the rise to power of Hitler forced him and so many other fellow Jews in the professions to seek refuge abroad. Reaching the United Kingdom before the second world war started, he was appointed to the staff of the chest clinic, Kingston upon Hull, in 1940, serving first as tuberculosis officer and later as assistant chest physician (S.H.M.O. grade) until his retirement in 1955. Endowed to the end with youthful mental vigour and an inquiring mind in medical matters, especially those concerning chest disease, Dr. Dunner opted to continue voluntarily after retirement the medical work and investigations he had inaugurated in Hull. Under the sponsorship of the Leeds Regional Hospital Board, an industrial chest diseases clinic was set up, of which he was honorary medical director from 1955 to his sudden death.

Cosmopolitan, multilingual, and equally at home in any European capital, Dr. Dunner had never visited the U.S.A., but I know that his election a few years ago to honorary membership of the American College of Chest Physicians was an event that delighted him. He was the author of several textbooks. The last, *Clinico-radiological Differential Diagnosis of Lung Disease*, is now in its second German edition, and Dr. Dunner was occupied right up to the time of his death in preparing its English equivalent, which he hoped to publish. Apart from this and other books, he wrote a great number of papers, about 140 during his professional career. But it is not by his teaching and authorship that he will wholly be remembered. He was the first chest physician in Hull to look down a thoracoscope and use adhesion-section as a technique in the management of artificial pneumothorax. His logical mind and insatiable medical curiosity impelled him, where possible, to follow his difficult chest cases to the final arbitration of the post-mortem room. It was thus that he proved, for the first time, in a few industrial groups—boiler-scalers, "blue" (ultramarine) and graphite workers—that some of these operatives could acquire pneumoconiosis. These trades were subsequently "scheduled," so as to carry legal rights of compensation under the Industrial Injuries Acts.

A loyal and esteemed colleague, wise physician, and true friend, to whom I owe much, Dr. Lasar Dunner was by nature reserved and quiet-living, completely immersed in his medical work. Outside this his interests were literary, musical, and in the joys of travel, usually by air. He will be long remembered in the city and county of his adoption by all of us, including many grateful patients among Hull's industrial male population. Generous and unsparing of himself on their behalf, his work in pneumoconiosis is his "monument more perennial than bronze," that will endure beyond the lifetime of them and of ourselves.

N. J. ROCHE, O.B.E., M.R.C.S., L.R.C.P.

Group Captain N. J. Roche, who was successively a medical officer in the Royal Navy and in the Royal Air Force and then a general practitioner, died suddenly at Bideford, Devon, on July 17. He was 84 years of age.

Nelson Joseph Roche was born on April 24, 1875, and received his medical training at Charing Cross Hospital. After qualifying M.R.C.S., L.R.C.P. in 1899 he entered the Royal Navy and progressed through the now obsolete ranks of surgeon, staff surgeon, and fleet surgeon. In 1918 he transferred to the Royal Air Force with the old rank of lieutenant-colonel, and served for five years, attaining the rank of group captain. For his services in the first world war he was appointed O.B.E. in 1919. During the course of his career in the R.A.F. he was principal medical officer in the north-eastern and coastal areas and in Iraq. From 1923 to 1952 he was in general practice at Southsea, becoming also honorary consulting anaesthetist to the Portsmouth Eye and Ear Hospital. He served on the Council of the British Medical Association from 1926 to 1930 as the representative of the Royal Air Force Medical Service, and was a member of the old Naval and Military Committee over the same period.

R. A. D. writes: I first met Nelson Roche when he was a staff surgeon in the Royal Navy serving in Portsmouth many years ago. We met again during the second world war. On retiring from the R.A.F. he joined me in partnership, and remained in practice until the death of his wife in 1952, when he retired. He then went to live near his daughter at Instow, North Devon, where he is buried in the village cemetery. A great sportsman, he was one of the most kind-hearted men I have ever met; many at Southsea will remember him with affection.

HARRY WALKER, L.R.C.P.&S.Ed., F.F.A. R.C.S.

Dr. Harry Walker, consulting anaesthetist to the Tees-side group of hospitals, died suddenly in hospital on July 18 in his fortieth year.

Harry Walker was the eldest son of a well-known Middlesbrough dentist. After qualifying at Edinburgh in 1942, he held the post of house-surgeon at the North Riding Infirmary, Middlesbrough. During the second world war

he served with the R.A.M.C. in Burma and Java, and on demobilization he entered general practice in Middlesbrough, first as assistant and later as partner in the practice of Drs. Clark, Fleischmann, and Walker. Always interested in anaesthetics, he took the Diploma in Anaesthetics in 1948, and shortly afterwards gave up general practice when he was appointed consultant anaesthetist to the Tees-side group of hospitals. He was admitted F.F.A. R.C.S. in 1954.

Harry Walker was a man of unfailing courtesy and cheerfulness, and his untimely death has come as a great shock to his friends and colleagues on Tees-side. He is survived by a widow and three young daughters.

RONALD SILCOCK, M.R.C.S., L.R.C.P., D.T.M.

Dr. Ronald Silcock, a well-known general practitioner in West Hampstead, died on July 21 at the Hospital of St. John and St. Elizabeth, after a short illness. He was 69 years of age.

Ronald Silcock was born in Harley Street on December 23, 1889, the son of Dr. A. Quarry Silcock, a surgeon attached to St. Mary's Hospital and to Moorfields. He was educated at Blundells, and qualified M.R.C.S., L.R.C.P. from St. Mary's Hospital in 1914. He served as a dresser with the British Red Cross Society in the Balkan war of 1912–13, and held commissions in the Army and Royal Navy in the first world war. After discharge from the Army he took the Diploma in Tropical Medicine in 1921, and spent some time in India and Ceylon. Returning from India in the early nineteen-twenties, he came to West Hampstead, where he was in practice for the rest of his life.

D. K. M. writes: The many friends of Ronald Silcock feel a deep sense of loss at his passing. Endowed with great energy and ability, he conducted a successful practice in West Hampstead, and he was conscientious to a degree in looking after his patients. As a result he became beloved by all, and his loss will be greatly felt. He leaves a widow, to whom our deep sympathy is extended.

F. P. MYLES, M.B., B.Ch.

Dr. F. P. Myles, who practised at Wisbech, died on August 1, aged 40.

Frederic Peter Myles was born on July 1, 1919, and graduated M.B., B.Ch. at Trinity College, Dublin, in 1946. After holding the appointments of house-surgeon and resident anaesthetist at the Royal Gwent Hospital, Newport, he entered general practice at Wisbech, becoming also anaesthetist to the North Cambridgeshire Hospital.

W. H. C. writes: With the sudden passing of Peter Myles a great loss has been sustained by the borough of Wisbech. For the last 10 years he unstintingly gave of his best both as a general practitioner and as an anaesthetist at the hospitals. In the former capacity he was the kindly, assiduous friend of his patients, and in particular was beloved by the many children who constituted a large proportion of his practice. As an anaesthetist he was only satisfied with the highest standards, as was evidenced by his technical skill. His efforts to provide safety for the patients in his care were exemplified by his scrupulous pre-operative assessments and by an equally thorough attendance in the recovery phase. Personal exhaustion was willingly accepted in his determination to live up to his ideals. In early adult life a period of serious ill health and enforced leisure had given him the opportunity to paint, and he became an artist of no mean ability. Indeed, the artistic side of his temperament was apparent in his work and formed an important element of his retiring personality. His sudden and tragic death leaves many sad hearts among his partners, patients, and hospital colleagues.

C. K. E. writes: Born in Bristol, Peter Myles was educated at Campbell College, Belfast, where he showed a considerable aptitude for games. It was while he was a medical student that a chance meeting with Julius Olsson touched off a lively interest in seascape painting, and he subsequently exhibited at the Royal Hibernian Academy. He entered group practice in Wisbech in 1949, and a consultant-practitioner appointment to the Wisbech hospitals enabled him to continue with anaesthetics, where his skill developed to an extent unusual in a part-time specialty. His continued interest in sport was shown by his being vice-commodore to the Hunts Sailing Club. A likable personality, he will be generally missed from the Fenland scene.

OSCAR FEHR, M.D., L.R.C.P.&S.Ed.

Professor Oscar Fehr, formerly head of the department of ophthalmology at the Rudolf Virchow Hospital, Berlin, and, later, an ophthalmic surgeon in practice in London, died in London on August 1, aged 87.

Born at Braunschweig, Germany, on October 9, 1871, Oscar Fehr studied medicine at the universities of Heidelberg, Berlin, and Kiel. Having graduated in medicine he decided to specialize in ophthalmology. He first became assistant to Professor Julius Hirschberg in Berlin, and then in 1907 was appointed chief of the eye department of the newly erected Rudolf Virchow Hospital in Berlin. In the course of the next few years under Fehr's outstanding leadership the ophthalmic department of the hospital was enlarged to 120 beds, and became the largest eye hospital in Berlin.

H. H. L. writes: It was at the Rudolf Virchow Hospital that Oscar Fehr, due to his quite exceptional operative skill as well as his devotion to duty and his feeling of responsibility towards his patients, built up his fame as the most brilliant eye surgeon of the Germain capital, and his reputation soon spread to many other countries. Apart from his hospital duties Fehr had a very large private practice. Working untiringly from early morning till late at night, he showed human understanding and the greatest kindness to all his patients. Fehr had published more than 45 important papers, and did much postgraduate teaching. In 1919 he was awarded the title of professor.

In 1934 the Nazis forced Fehr to resign from the hospital. Further restrictions and humiliations which this great man had to endure resulted in his departure from his native land, and he arrived in this country together with his family shortly before the outbreak of the second world war. Some time later he became a student again in order to obtain the Scottish triple qualification, and he passed his finals in 1943 at the age of 71 years. He was then allowed to establish himself as an ophthalmic surgeon in Harley Street, and his practice in London was from the outset enormous. His Continental patients flocked to him, and also many English patients asked for his advice and help. His youthfulness and good health allowed him to operate until the age of 80. The last few years of his life were saddened through illness; this was especially tragic when his own sight began to fail, and towards the end he became practically blind. Apart from his profession, to which he was so devoted, Fehr had many interests. He was an excellent amateur painter, he loved music and the arts, and read widely. He was a man of the highest integrity, noble in character, brilliant in his profession, and modest in his demeanour. He will be sorely missed by his many friends and patients, and will never be forgotten.

PHILIP LAVERY, M.B., Ch.B.

Dr. Philip Lavery, who was in general practice in Cardonald, Glasgow, died suddenly on August 1, aged 64.

Philip Lavery was born on December 5, 1894. During the first world war he transferred from the Yeomanry to the Royal Flying Corps, in which he was commissioned. His active flying duties continued until he was wounded towards the end of the war. He did not take up medicine until he had explored the possibilities of other careers, for after a spell in Malaya as a rubber planter he entered the printing ink industry in Glasgow. In 1929 he married Miss Margaret

Curran, B.Sc., a lecturer in geology, and a year or two later they decided to study medicine together. He graduated M.B., Ch.B. at the University of Glasgow in 1937 and remained in practice in Glasgow until his death. He was an active member of the local medical committee and of the Glasgow and West of Scotland Branch of the B.M.A.

C. M. writes: By the sudden death of Dr. Phillip Lavery, Glasgow has lost one of her most colourful medical personalities. When he decided to study medicine with his wife he started from scratch and tackled the work with his usual zest: they both completed the course successfully. He practised for 20 years in the Cardonald area until a severe operation curtailed his activities, and he took time off for two voyages to the East with the Blue Funnel Line. He had travelled extensively: more than 30 years ago he visited the Mayo brothers at their clinic. He had a keen interest in human nature and was a born organizer. His practical help and encouragement to young doctors was prodigal. This short, dynamic figure with his fine head of silver hair, his shrewd comment, and his fund of anecdote will long be remembered by his many friends and colleagues. He is survived by his wife, Dr. Margaret Lavery, to whom we extend our sincere sympathy.

D. A. M. ELLIS, M.B., B.S.

Dr. Dudley Ellis, surgical registrar at Barnet General Hospital, died in Boscombe Hospital on August 9, aged 29.

Dudley Anton Millard Ellis, the son of Mr. and Mrs. Robert Ellis, of Bournemouth, was born in London on December 18, 1929. Educated at Cranleigh School, King's College, London, and the Westminster Hospital, he qualified in 1953 and graduated M.B., B.S. in the following year, obtaining honours in therapeutics. At the Westminster he was prominent in student activities, being secretary of the music society and captain of athletics. He held resident appointments at the Westminster, St. Stephen's, the Royal Marsden, and Great Ormond Street Hospitals, and in 1959 he took the M.R.C.P. Intending to specialize in thoracic surgery, he passed the primary F.R.C.S. examination, but illness intervened before he could complete the final examination. Our sympathy goes to his parents and his fiancée in their tragic loss.

Medico-Legal

ARBITRATION CLAUSE IN PARTNERSHIP AGREEMENTS

[FROM OUR LEGAL CORRESPONDENT]

On June 3 the Court of Appeal gave judgment in a case (*Finer* v. *Melgrave*) between two doctors in partnership where one of them had sought to terminate the partnership by an action in the courts. The two doctors, A and B, had entered into partnership in 1948 under a deed containing the usual arbitration clause. Subsequently a dispute arose between them, and Dr. A began an action in the Chancery Division to dissolve the partnership. Dr. B applied to the court to have the action stayed and to compel Dr. A to rely on the arbitration clause for his remedy. The judge refused the application (*The Times*, February 18). Dr. B then appealed, but the Court of Appeal upheld the judge's refusal (*The Times*, June 4).

An arbitration agreement may be worded in such a way as to amount to an attempt to oust the jurisdiction of the court. At Common Law, before the position was modified by Statute, agreements so worded were held to be ineffective. By an arbitration agreement the contracting parties could agree that questions of law and fact should be decided by some person instead of by a court of law. They could go so far as to make that person the final arbiter on questions of fact. But they could not deprive themselves, at Common Law, of the right of recourse to the courts on questions of law. However, by the Arbitration Act, 1950, the courts have discretionary power to give effect to agreements which formerly would have been ineffective by making an order, at the request of one of the parties to the agreement, staying an action brought in contravention of the agreement. It was once thought that the courts would never exercise this discretion to stay court proceedings for dissolution of a partnership, but that is now known not to be so.

Reasons for Refusal

In the case of *Finer* v. *Melgrave* a stay of action was refused on three grounds. First, issues of law were involved, and although this was not conclusive it was a persuasive factor. Secondly, the substantial issues of fact between the two doctors also gave rise to a claim against the wife of one of them, who not being a party to the arbitration agreement would not be bound by the arbitration. Thirdly, there had been a long lapse of time, and the sooner the matter was disposed of the better. It was the view of the Chancery judge (and the Court of Appeal was not disposed to say that he had failed to exercise his discretion on good grounds) that these considerations overrode the weighty consideration that it was in the interests of the parties concerned and of the medical profession that matters of this sort should not be ventilated at a public trial, especially as some patients would have to be called to give evidence.

The refusal of the Court of Appeal to allow the appeal does not mean that the judges of that court would have exercised the discretion in the same way. Where the judge is given a discretion, the Court of Appeal will not reverse his decision unless he has exercised that discretion on a totally wrong principle, or has failed to exercise it at all. The Court of Appeal will not attempt to substitute its discretion for that of the trial judge.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Dr. G. S. Brindley has been appointed a University Lecturer in the Department of Physiology with tenure from October 1, 1959, for three years.

In Congregation on June 13 the following degrees were conferred:

M.D.—J. H. Angel, J. E. MacIver, M. J. Purves.
M.B.—Margaret U. Bullen, Andrea M. D. Langford, P. O. Liebling.

Sir George Pickering, Regius Professor of Medicine in the University of Oxford, was elected to an Honorary Fellowship of Pembroke College on June 1.

On June 8 Sir Alan Drury, former Director of the Lister Institute and former Fellow of the College, was elected into an honorary Fellowship of Trinity Hall.

UNIVERSITY OF GLASGOW

The following degrees were conferred on July 4:

M.D.—[1]W. M. Borthwick, [2]M. K. Browne, [1]W. A. J. Crane, [2]J. Macvicar, S. D. S. Park, [2]G. Sclare, [2]T. S. Scott, [1]A. N. Smith.
CH.M.—[1]H. L. Duthie.
PH.D.—T. A. H. Pasieczny.
M.B., CH.B.—C. L. Adeoye, O. M. Adeyemo, C. L. Ahara, J. B. B. Asafu-Adjaye, I. C. Balfour, N. Baxter, A. Bennett, E. H. Berman, Anne M. S. Black, A. E. Blitz, Nicolette A. Brandt, Marjorie P. Brown, Frances B. Buchan, H. J. Calder, Kathleen Calder, L. Cameron, Toh-Yong Chong, A. J. Cochran, J. D. Crosbie, R. L. C. Cumming, Beryll J. Dean, A. S. B. Dickson, Laura M. Dodds, W. M. Doig, A. C. I. Duncan, I. Duncan, J. Fairbairn, D. W. Ferguson, J. C. Ferguson, W. Forbes, A. D. Fraser, I. D. O. Frew, T. A. Gellatley, G. Gillespie, D. M. Goldberg, [1]A. Gorchein, Jean A. Gow, J. Graham, J. A. Grogan, J. S. H. Hamilton, J. Hanna, D. McK. Hart, Ann McK. Hay, N. A. Hogg, G. D. Ikedife, I. T. Jackson, J. M. Jackson, K. Keczkes, I. A. Kennedy, R. D. Kennedy, Wavnie P. Kum, R. Limpitlaw, T. S. Little, [2]R. G. Luke, [2]T. A. McAllister, J. H. Macartney, J. C. McBride, Mary McBride, Grace V. McCaffer, J. McCall, C. McCreadie, Helen P. McEwan, C. G. McKay, N. MacKay, H. D. MacLeod, Sheila M. J. Macleod, Elizabeth D. S. McMillan, [2]J. McNeil, R. C. McQueen, Elspeth L. Macrae, R. N. Macl. MacSween, I. W. S. Mair, G. Mallon, R. Marks, W. J. S. Marshall, W. M. P. Mauchline, J. R. M. Murdoch, [2]D. Murray, I. MacL. Murray, [2]A. M. Neville, Patricia A. S. Nicholson, Johanna A. Nicholson, Constance M. Noble, S. Ofosu-Amaah, T. W. Parsons, Daphne H. Pyle, C. J. Quigley,

Jean A. S. Rankin, W. S. M. Robertson, Natasha Rose, Margaret S. Ross, R. MacF. Ross, J.Runcle, Agnes S. L. Scoulier, J. C. Semple, T. Sikanartey, R. R. Smith, T. E. Steven, A. M. Sutherland, A. P. Thomson, Janette I. Vincent, M. Wallace, A. M. Watson, Christina H. Wilson, J. M. Wilson, F. W. Wittmann, I. H. Y. Wood, R. J. Woodhouse, E. T. Young.

[1]With honours. [2]With commendation.

On June 22 the degree of M.D. was conferred, *in absentia*, upon F. W. Campbell (with commendation), T. H. C. Barclay, and Mrs. Janet J. Jellard (née Mackintosh) (with commendation).

On June 26 the Diploma in Public Health was awarded to J. C. Baird, W. M. Buchanan, D. R. Edmiston, Stella E. G. Gibson, R. G. Haughie, G. P. Henry, S. J. Lepper, Catherine S. MacGregor, Ruby McMillan, J. M. Paterson, D. A. Player, Margaret D. Thomson, J. G. Young.

UNIVERSITY OF EDINBURGH

Dr. J. W. B. Douglas, Senior Lecturer in Public Health and Social Medicine, has been admitted to the status of Reader, with effect from October 1, 1959.

Dr. A. Rae Gilchrist, Reader in Clinical Cardiology, has been admitted to membership of the Senatus, as representative of the Faculty of Medicine, for a period of two years from October 1, 1959.

The University Court has conferred honorary status as follows: *Honorary Lecturer in the Department of Bacteriology*, Dr. Mary McMillan. *Honorary Assistant in the Department of Orthopaedic Surgery*, Dr. Anne E. Perry. *Honorary Research Assistant in Department of Surgical Science*, Henry Gewurz, B.A. (Indiana School of Medicine).

The following appointments are announced: Dr. A. G. C. Renwick, Lecturer in Bacteriology; Dr. Mavis Wakefield, Part-time Lecturer in Child Life and Health; Dr. W. P. Thomson (Part-time Lecturer) and Dr. John Walker (Lecturer) in General Practice Teaching Unit; Dr. S. H. Taylor and Dr. E. A. Harris, Lecturers in Medicine.

Dr. I. W. B. Grant resigns his appointment as honorary Lecturer in Tuberculosis as from October 7, 1959.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following candidates have been approved at the examinations indicated:

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part I*: M. White. *Part II*: T. Asuni, K. E. Dewhurst, Brenda R. Montgomery.

The following degrees and diplomas were conferred on July 2:

M.D.—Mary E. Martin.
M.A.O.—I. J. Dalrymple.
L.M., L.Ch., L.A.O.—R. A. H. Mooney.
M.B., B.Ch., B.A.O.—C. C Bamber, J. W. Bennett, Angela N. Buddery, Yam Mui Chee, B. Cronin, Judith J. Cuthill, J. A. Doherty, J. M. Dunlop, E. C. Emekekwue, J. H. English, K. J. Gibbons, Ann R. E. Gibson, M. Goldberg, M. O. Grant, P. McN. Hill, J. H. Holroyd, Jane M. Jackson, W. S. Jagoe, J. D. Jessop, M. G. C. Kelly, P. G. Kernohan, K. O. Labinjo, W. E. Lavelle, M. A. Lewis, Elisabeth M. Lurring, Marjorie J. McCarthy, K. J. G. McCourt, Grace J. McM. McCurdy, D. W. S. Mason, Ann G. Mould, H. S. O'Connor, O. I. A. Onojobi, J. M. W. Orr, M. F. N. O'Ryan, Oonagh A. B. Redmond, M. Lloyd Roach, D. W. A. Rosser, H. B. Smith, P. A. Tan.

UNIVERSITY OF DURHAM

In Congregation on July 3 the honorary degree of D.D.Sc. was conferred on Sir Wilfred Fish, M.D., F.D.S. R.C.S., President of the General Dental Council.

In Congregation on July 3 and 4 the following degrees and diplomas were conferred:

M.D.—Millicent Payne, R. O. K. Schade, C. G. Tulloh, J. H. Walker, *D. Whitehouse.
PH.D.—*In Medicine*: Anne P. Jobling, B.D.S., *Angel H. Zaki.
M.B., B.S.—W. J. Atkinson, H. Anker, Shirley M. Arthur, J. M. Barker, D. W. Bethune, Lily Burn, Hazel Butler, H. Campbell, I. Capstick, A. M. Carr, D. W. Chapman, Mary E. Cheshire, J. Croudace, Ann M. Crump, Elspa C. Davies, P. M. J. J. Dee, D. W. Forster, Lorna A. Gregory, Judith M. Heron, W. A. Hewitson, F. A. Ive, M. A. Izadi, P. A. Johnson, L. J. Kinlen, J. R. Kirkpatrick, Nii-Osa Kwao, C. J. N. Lawson, I. G. Lloyd, J. M. McLean, T. R. Martin, C. Maunder, I. A. Miller, R. A. Moffett, T. E. Nelson, J. K. Owusu-Ansah, D. T. Pearson, Elisabeth V. Rafique, T. Reynolds, T. J. Richards, A. M. Robson, G. D. Shapero, W. Y. Sinclair, Margaret Slater, S. Steel, Sheila Stein, Frances E. Thompson, J. B. Wade, C. Waine, J. R. Waring, F. Wills, Anne H. Young, *C. D. Caplan, *A. Sai-Yee Chao, *I. A. Drysdale, *Margaret K. Huddart, *O. B. Onibuje, *K. Varde.
DIPLOMA IN PSYCHOLOGICAL MEDICINE.—P. L. Kalra, P. Morgan.
**In absentia.*

UNIVERSITY OF LONDON

Dr. M. I. A. Hunter has been elected the additional representative of the Faculty of Medicine on the Senate until May, 1964.

The Sir William Dunn Scholarship for 1959 has been awarded to Anthony David Hoyes (St. Mary's Hospital Medical School).

The Hazel Clifford Postgraduate Studentship for 1959 has been awarded to Mrs. Gillian Barbara Brunton, M.B., B.S. (Middlesex Hospital Medical School).

On June 17 the degree of M.D. was awarded by the Senate to Gerald Sandler.

Mr. J. B. Hume has been elected chairman of the Council for External Students for the remainder of the year, 1958–9, in succession to Dr. S. J. Worsley.

Dr. E. C. Warner has been nominated for appointment as representative of the University on the governing body of the West London Hospital Medical School.

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *Institute of Obstetrics and Gynaecology*, Dr. H. P. Ferreira (Pathology); Dr. I. F. Sommerville (Biochemistry); Mr. G. Wynn-Williams (Obstetrics and Gynaecology). *Middlesex Hospital Medical School*, Dr. R. W. Gilliatt (Medicine (Neurology)). *St. George's Hospital Medical School*, Dr. H. Stern (Probationary recognition as a teacher of Pathology (Bacteriology) for two years from March, 1959).

The degree of M.D. has been awarded to Dr. D. B. Shaw, J. Eastwood, and P. Jordan.

UNIVERSITY OF MANCHESTER

The following candidates have been approved at the examinations indicated:

CH.M.—W. W. Wilson.
FINAL M.B., CH.B.—[1] [2]P. H. Fentem, J. M. Anderton, Gillian A. Appleton (née Goldstone), D. A. Ashworth, Dorothea P. J. Badger, G. C. Bentley, D. C. Beton, P. J. Beynon, Elizabeth H. Bradbury, A. K. Brown, D. Charlesworth, T. A. Cook, J. W. Crossley, N. C. Eccles, F. R. Ellis, H. B. Fearnley, Sylvia M. Francis, R. Gamble, J. B. Garland, Jill N. Gordon, R. A. W Guthrie, [3]J. D. Hamlett, D. W. Holden, Shirley Holt, J. W. Hope, P. Hughes, P. W. Jackson, T. P. Johnson, Margaret G. Jones, J. H. Kilshaw, Astrida Lambergs, Moraig Leslie, P. N. McIntyre, Beryl Melton, G. F. Mills, [2]G. Milner, J. C. Milner, J. R. S. More, J. J. Nattrass, G. P. R. Ogilvie, D. R. Petchey, C. J. Riley, Jean Ritchie, J. K. Roberts, R. M. Sandler, B. A. Sides, Maxine Staniford, Maureen Statham, E. P. Trowler, Lilian Tyers, G. K. Vanner, [3]H. Wacks, P. B. Walsh, J. Wanka, R. Wann, G. White, Ann Wrigglesworth.
[1]With honours. [2]Distinction in obstetrics and gynaecology. [3]Distinction in surgery.

UNIVERSITY OF WALES

The following candidates at the Welsh National School of Medicine have satisfied the examiners at the examination indicated:

TUBERCULOUS DISEASES DIPLOMA.—C. A. Q. M. Badruddoza, S. C. Banerjee, M. Gooran, K. S. Halaby, M. H. Husaini, A. M. Jayousi, T. R. Jones, D. S. Karandikar, Y. Lakshminarayana, O. O. Makanjuola, T. J. Malherbe, K. P. Mankani, N. L. Maskay, Rao Narayana (with distinction), That-Tze Ng-Lun, N. C. Saha, A. M. Selvaraj, S. S. A. Shah, P. Visalvethaya, M. C. T. Waas, M. I. Yad.

In Congregation on July 17 the following degrees were conferred:

M.B., B.CH.—P. J. Atkins, Joan Bishop, F. M. Cole, Eluned Davies, H. L. Davies, Lorna E. Elliott, Helen B. Farrar, W. E. Fine, Joan I. Francis, H. A. Goodwin, H. Hopkins, E. G. Hoyen Chung, Eluned M. Hughes, L. Hughes, Edna M. Jacoby, Hannah D. Jenkins, G. Johns, Aileen Jones, Beryl I. E. Jones, E. J. Jones, Helen L. Jones, Mair Jones, P. E. Jones, W. M. Jones, B. C. Lentle, C. T. Man-Son-Hing, Elizabeth R. Mendl, D. B. Morgan, J. Pegington, Anne Rees, Marion H. Rees, E. H. Reynolds, Elwyn Roberts, Jessie M. A. Rogerson, R. C. Ryder, T. J. Stamps, A. E. Walton, Corinna M. Weaver.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

M.D.—D. Annis, Winifred J. A. Francis, F. D. Kitchin, B. W. McGuinness, G. W. Pennington, H. Wilson.
CH.M.—Frances Selsnick.
M.B., CH.B.—[1] [2]Elizabeth M. Higham, [1] [3]M. H. Lader, [1] [2]E. Tapp, M. H. Abenson, C. N. Ashcroft, Rachel M. Bartlett, P. J. R. Bell, R. E. Bourdillon, J. R. Brew, N. J. M. Brown, P. W. Brunt, J. K. Campbell, H. Casson, W. G. Coddington, J. M. Davies, J. T. Dawson, R. Duckworth, J. A. Edwards, Patricia M. Frankland, Janet G. Halley, B. T. Harris, Janet Hawcroft, A. Hawe, T. M. Hayes, F. S. Heard, K. G. Hine, Marguerite P. Holley, F. A. Howard, T. A. Hyde, M. H. Irving, F. J. Jarrett, A. F. Jones, M. Kewley, A. H. Lewis, B. V. Lewis, J. A. Lister, R. Lynch, Mary P. McCarthy, G. S. Makin, A. R. Mawdsley, W. P. Merrick, A. C. Murphy, D. Murphy, G. O. Obu, J. J. T. Owen, Jane C. Parkes, M. J. T. Peaston, B. T. Pitt-Hart, Audrey M. Platt, T. G. Price, H. F. V. Riddle, M. A. Ross, Jeannette A. Smith, Colette Taylor, Joan M. Thomas, Dorothy E. A. Thompson, E. E. M. Thompson, Joyce M. Towers, Ruth J. Turner, J. L. Verbor, Wena V. P. Williams. *Passed in separate subjects*: G. Balderstone, J. H. Lloyd, and Patricia A. Moore (surgery and obstetrics and gynaecology); K. R. Ball, T. D. Birtles, J. A. Q. Blukoo-Allotey, Essillt Evans, and R. Pactor (medicine and obstetrics and gynaecology); Judith M. Burgess, K. Cartwright, B. H. E. James, and C. J. Merry (medicine and surgery).
DIPLOMA IN PUBLIC HEALTH.—A. Afnan, J. A. Black, Jean O. R. Carmichael, Irene L. Chesham, Irene M. J. Cox, J. S. Doyle, G. P. Evans, Madge Farmer, A. J. Graham, J. R. Jones, J. Keane, W. Manwell, S. R. W. Moore, D. R. Morris, June Nelson, J. O'Gorman, Gladys I. Wilson, H. E. Wilson, Margaret T. Wood.
DIPLOMA IN RADIOLOGY.—*Radiodiagnosis*: M. A. Bloomfield, A. Dutt, N. Geffen, P. P. Keith, M. I. M. Nilar, R. A. Owen, H. P. Tulloh. *Radiotherapy*: A. Kumar, B. N. Roy.
[1]With second-class honours. [2]Distinction in surgery. [3]Distinction in medicine.

UNIVERSITY OF LEEDS

Dr. G. M. Lewis has been appointed temporary lecturer in the Department of Paediatrics and Child Health for a period of two years from October 1, 1959.

Dr. A. N. MacPhail has been appointed Senior Lecturer in the Department of Preventive Medicine and Public Health from September 1, 1959.

The following candidates have been approved at the examinations indicated:

M.D.—K. Sanders.

CH.M.—M. N. Tempest.

M.B., CH.B.—E. M. Asare, G. G. Bird, I. B. Copley, M. J. Fitzpatrick, J. D. Gomersall, B. G. Gray, R. D. Hall, S. S. E. Hassan, Constance M. Hunter, Margaret M. Johnson, B. E. Marshall, J. E. Marshall, A. I. Oglesby, A. I. Onukugu, Barbara J. Pollard, H. L. Proctor, J. N. Rogers, L. F. G. Schiller, N. Soloff, Eileen D. Watkins.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—D. G. Brown (with distinction), M. Frieze, A. I. Roith.

UNIVERSITY OF SHEFFIELD

The following appointments were made on June 19: Dr. C. E. Blank, full-time Lecturer in Medical Genetics; Dr. D. Macmillan, part-time honorary Lecturer in Psychiatry; Dr. D. Verel, part-time Lecturer in Cardiology.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

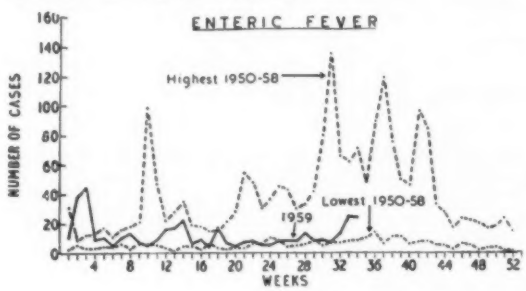
At a meeting of the general body of Fellows of the Royal Australasian College of Physicians held in Adelaide on May 27, the following were elected and admitted to Fellowship of the College: *Under Article 44:* J. C. Belisario, of New South Wales, and Muriel E. Bell, of New Zealand. *Under Article 42:* D. A. Ballantyne, J. V. Cable, O. W. Chapman, J. A. K. Cuningham, A. O. M. Gilmour, D. McR. Hanna, J. R. Hinds, K. H. Holdgate, J. A. Kilpatrick, E. G. McQueen, and J. L. Newman, of New Zealand; M. W. Fletcher, of Tasmania; Leo Flynn, R. L. Harris, P. J. Markell, and Willa Nelson, of New South Wales; H. R. Gilmore, of South Australia; Bryan Hudson and W. Hamilton Smith, of Victoria; W. B. Macdonald and W. R. Pitney, of Western Australia.

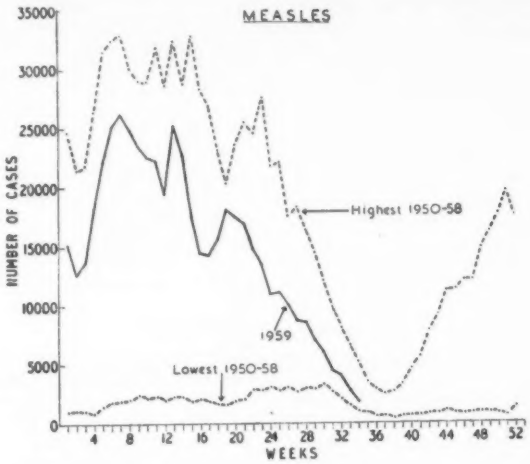
The following candidates, who were successful at an examination held in Australia, were admitted to Membership of the College on May 27: James C. Biggs, T. Burfitt-Williams, Alan H. B. Chancellor, E. G. Cleary, W. R. Hobart, J. E. Jefferis, David Jeremy, Graeme J. Morgan, John J. Morgan, M. R. Playoust, James Rankin, and F. X. M. Willis, of New South Wales; W. C. Boake, H. D. Breidahl, J. A. Brenan, K. D. Muirden, James R. Syme, D. C. Wallace, and J. S. Yeatman, of Victoria; Peter S. Hetzel, G. A. Hunter, and J. L. Waddy, of South Australia; M. J. Eadie, of Queensland; Max N. I. Walters, of Western Australia. E. S. Finckh, of New South Wales, and R. T. W. Reid, of South Australia, were admitted to Membership under the provisions of Article 37.

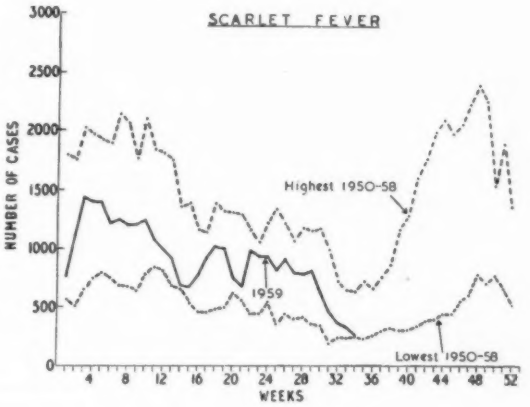
Vital Statistics

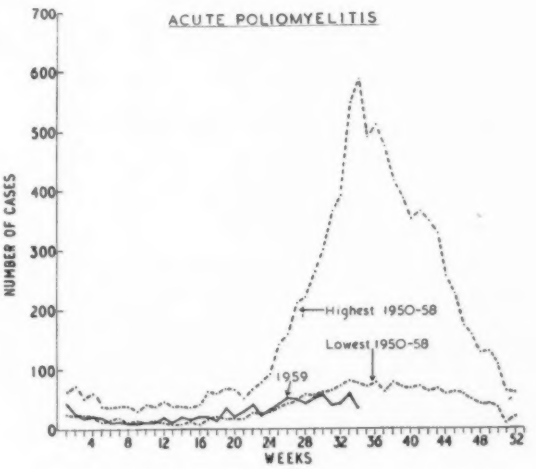
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1950–8 are shown thus ------, the figures for 1959 thus ———. Except for the curves showing notifications in 1959, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Typhoid Fever in County Londonderry

An outbreak of typhoid fever occurred during July and August at Ballyreagh, which is part of the coastal area between Portstewart (Co. Londonderry) and Portrush (Co. Antrim) and which is a popular site for caravans and temporary dwellings. We are indebted to Dr. J. H. BREWSTER, county medical officer of Londonderry, for the following details. The number of confirmed cases amounted

to 29 (16 males and 13 females). There have been no deaths so far and the disease has been of mild or moderate severity. The ages of the patients ranged from 5 months to 60 years. There were 25 primary cases and 4 secondary cases. Every county in Northern Ireland had cases or suspects among those who had been on holiday in the area.

The causal organism was *B. typhosus*, phage type C1. The source of the epidemic was believed to be a male carrier who had infected the water in a local well in Young's field. A heavy downpour of rain on July 18 ended a dry spell and is thought to have washed infected material down into the well. In Young's field at the time there were 50 temporary hutments and about 67 caravans.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment was reported in July was 94, compared with 94 in the previous month and 68 in July, 1958.

The numbers of cases of industrial diseases in the United Kingdom reported during July were as follows: Lead poisoning 7, aniline poisoning 4, arsenical poisoning 1, compressed-air illness 6, epitheliomatous ulceration 26, chrome ulceration 11; total 55. There were no deaths.—*Ministry of Labour Gazette*, August, 1959.

Week Ending August 29

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available

	Week ending Aug. 22	Aug. 29
Dysentery		
Lancashire	72	67
Liverpool C.B.	9	14
Radcliffe M.B.	3	10
Blackburn R.D.	7	14
London	47	37
Kensington	1	10
Warwickshire	37	53
Birmingham C.B.	11	15
Coventry C.B.	19	27
Yorkshire East Riding	28	32
Kingston-upon-Hull C.B.	28	32
Haltemprice U.D.	12	14
Yorkshire West Riding	43	44
Leeds C.B.	20	19
Acute Poliomyelitis		
Essex	4	5
Hampshire	10	2
Southampton C.B.	3	2
London	15	8
St. Pancras	0	3
Lancashire	1	5
Liverpool C.B.	1	3
Food-poisoning		
Cornwall	0	26
Penzance M.B.	0	26
Lancashire	60	81
Blackpool C.B.	20	26
Liverpool C.B.	13	23
Paratyphoid Fever		
Glamorganshire	0	3
Cardiff C.B.	0	3
Typhoid Fever		
Lancashire	0	2
Barrow in Furness C.B.	0	1
Leigh M.B.	0	1

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **August 22** (No. 33) and corresponding week 1958.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1959 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	1958 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	2	2	1	0	0	
Dysentery	385	47	179	8	6	338	54	138	16	3
Encephalitis, acute	2	0		0		6	2		1	
Enteric fever: Typhoid	8	3	0	23	2	4	0	1	0	
Paratyphoid	17	1	1(B)	0	1(B)	5	0	1(B)	0	2(B)
Food-poisoning	250	31	13	1		287	28	5	2	
Infective enteritis or diarrhoea under 2 years				20	48				9	22
Measles*	2,778	90	25	19	55	5,102	283	11	18	17
Meningococcal infection	16	1	9	3	1	9	1	8	0	1
Ophthalmia neonatorum	31	6	6	0		16	1	8	0	
Pneumonia†	115	4	94	1		183	12	98	3	1
Poliomyelitis, acute: Paralytic	34	11	1	0	2	57	3	23	1	15
Non-paralytic	24	4	2			29	2			
Puerperal fever§	214	39	7	0		237	30	13	1	
Scarlet fever	327	29	42	10	10	373	30	36	11	10
Tuberculosis: Respiratory	423	50	73	13		415	54	67	18	
Non-respiratory	53	2	13	3		75	9	13	6	
Whooping-cough	777	29	105	14	52	713	37	82	47	14

DEATHS	1959 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	1958 Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	1	0	0	8	0	1	1	0
Influenza	1	0	0		0	2	0	0	0	
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	367	30	17	8	1	300	19	11	9	
Poliomyelitis, acute	1	0		0	0	3	0		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory	62	5	7	2	1	60	8	9	0	2
Non-respiratory		1	2	1	0		0	0	1	1
Whooping-cough	0	0	0	0	0	0	0	0		0
Deaths 0–1 year	255	16	28	10	10	268	19	25	6	16
Deaths (excluding stillbirths)	8,168	601	507	108	107	8,187	649	514	88	133
LIVE BIRTHS	14,136	1205	950	269	367	14,009	1125	926	209	381
STILLBIRTHS	286	13	15			298	18	23		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Scholarships.—The Council of the British Medical Association invites applications for the following research scholarships:

Ernest Hart Memorial Scholarship (£300); *Walter Dixon Scholarship* (£300); *Ordinary Research Scholarships* (four of £200). The scholarships are given to candidates recommended by the Science Committee of the Association as qualified to undertake research in any subject (including State medicine) relating to the causation, prevention, or treatment of disease. In addition, applications are invited for the award of the *Insole Scholarship* (£250) for research into the causes and cure of venereal disease. Each scholarship is tenable for one year, from October 1. A current scholar may apply to be re-appointed for a further year, though no scholarship will be renewed more than twice. A scholar is not necessarily required to devote the whole of his or her time to the work of research, but may be a member of H.M. Forces or may hold a junior appointment at a university, medical school, or hospital, provided the duties of such appointment will not, in the opinion of the Science Committee, interfere with his or her work as a scholar.

Applications for scholarships, including renewals, must be made not later than March 1, 1960, on the prescribed form, a copy of which will be supplied on application to Dr. D. P. STEVENSON, Secretary, B.M.A. House, Tavistock Square, London, W.C.1. Applicants are required to give the names of three referees who are competent to vouch for their capacity for the research contemplated.

Doctors' Hobbies.—The Doctors' Hobbies Exhibition, sponsored by Benger Laboratories Ltd., will be held in the Great Hall of B.M.A. House from November 16 to 20. Last year's exhibition attracted over 500 entrants, and many unusual items were displayed. This year the classes have been revised and more clearly defined, giving a total number of 22. Metalwork is combined with engineering, and archaeology with natural history. A "Home Handyman" section, which is intended to attract the "do-it-yourself" experts, is introduced for the first time. The organizers would like to improve the antique section, and also hope that there will be a large display of models. Painting, photography, philately, woodwork, authorship, embroidery, and electrical work offer further scope. Cups will be awarded to the best exhibit in each of the 22 classes. Further prizes will be presented for the three outstanding exhibits in the exhibition. Doctors who wish to exhibit and who have not yet received or have mislaid their entry form should apply to the Public Relations Department, Benger Laboratories Ltd., Holmes Chapel, Cheshire. The closing date for entries is September 23.

Indecency with Children.—A draft Bill which would close a gap in the law concerning indecent conduct in relation to children has now been prepared. It seeks to give effect to the conclusions reached by the Criminal Law Revision Committee, who were asked by the Home Secretary in March this year to consider alteration in the criminal law to provide for the punishment of a person who, without committing an assault, "invites a child to handle him indecently or otherwise behaves indecently towards a child." The draft clause provides maximum penalties of six months' imprisonment, or a fine of £100, or both, on summary conviction, or two years' imprisonment on conviction on indictment, for "any person who commits an act of gross indecency with or towards a child under the age of 14, or who incites a child under that age to such an act with him or another." (*Criminal Law Revision Committee, First Report* (*Indecency with Children*), H.M.S.O., price 6d.)

"Nutritio et Dieta."—The idea of this new review devoted to the study of nutrition in man was suggested at a meeting of the "Journées Européennes de Diététique" held in Madrid in 1957, where it was agreed that, though there was no lack of publications on nutrition, the work done usually referred to animal experiments and the results could only very cautiously be applied to man. Manuscripts should be sent to Professor J. TRÉMOLIÈRES, Laboratoire de Nutrition Humaine de l'Institut National d'Hygiène, 3, Rue Léon-Bonnat, Paris, 16, or Dr. H. KAPP, 44, Holbeinstrasse, Basle, Switzerland. Corrected proofs, books for review, and all inquiries should be sent to the publishers, S. Karger Ltd., 25, Arnold-Böcklin-Strasse, Basle, Switzerland. The subscription rate is Sw.Fr. 30 or $7.20 a year.

Colonial Development and Welfare Grants.—During the last 13 years colonial development and welfare grants have amounted to £174,988,967. Of this, £160,510,172 was for development and welfare, and £14,478,795 for research. During the year April 1, 1958, to March 31, 1959, medical and health services received grants totalling £1,594,431. Other totals included £938,302 for schemes for water supplies and sanitation; £329,295 for welfare; £152,114 for medical research; and £334,687 for the construction of Mulago

[*Central Office of Information*

Hospital, Uganda. Since 1951 colonial development and welfare grants for the modernization and extension of Holberton Hospital, Antigua, Leeward Islands, part of which is shown above, have amounted to £136,779. Ancillary buildings such as nurses' quarters, a new surgical ward, seven private wards, a new kitchen, two operating theatres, an *x*-ray theatre, a psychiatric ward, and a separate tuberculosis ward have been added to the original hospital.

British Veterinary Association.—The Council of the association are to issue a new quarterly research journal, *Research in Veterinary Science*, which will be open to contributions from workers in veterinary, medical, and kindred fields. The editorial board includes several non-veterinarians, among them Sir ALAN DRURY, F.R.S., and the scientific editors will be Mr. H. E. HARBOUR, Dr. V. B. BROOKSBY, and Professor D. L. HUGHES. The first issue will be published in January, 1960 (25s. for a single issue, 90s. per annum to non-members of the B.V.A.), by Blackwell Scientific Publications, Ltd., Oxford, to whom inquiries should be addressed. Contributions should be sent to the Scientific Editor, 7, Mansfield Street, Portland Place, London, W.1.

Animal Cancer Registries.—In a paper read to the British Veterinary Association Congress at Folkestone on September 2, Dr. E. COTCHIN, Royal Veterinary College, London, suggested that animal tumour registries should be set up in different parts of the world to collect and collate material and help in epidemiological and other studies. He believed that a more detailed study of the types and geographical distribution of spontaneous animal tumours might throw some light on the general problems of cancer in man.

President of British Association, 1960.—Sir GEORGE THOMSON, F.R.S., Master of Corpus Christi College, Cambridge, and a Nobel Prize winner, has been elected president of the British Association for the Advancement of Science for 1960, and will assume office on January 1.

British Academy of Forensic Sciences.—A meeting was held at the Ciba Foundation on September 4 to explore the possibility of setting up a British Academy of Forensic Sciences. Representatives of many of the professions involved in forensic work, individually or through their

organizations, were present at the meeting, which was under the chairmanship of Dr. F. E. CAMPS. It was decided that there was a need for a body of this kind to provide co-ordination and a common forum for the wide range of sciences involved. A steering committee is being set up and further information will be available later.

Handicrafts of Mentally Handicapped Children.—This year for the first time mentally handicapped children have entered their work in competitions sponsored by the Seventh International Handicraft and Do-it-Yourself Exhibition at Olympia, and have won several prizes in competition with normal children. The work includes embroidery, knitting, basketwork, soft toys, lamps, and lamp-shades. Officers of the National Society for Mentally Handicapped Children will be on duty on Stand 80 to give information until the exhibition closes on September 18.

College of General Practitioners.—Entries for this year's Butterworth Gold Medal essay competition, "The Child is Father of the Man," should reach the chairman of the awards committee, the College of General Practitioners, 41, Cadogan Gardens, London, S.W.3, by September 19.

"Nutcracker Man."—Dr. L. S. B. LEAKEY, curator of the Coryndon Museum, believes that a skull with huge teeth found by him and his wife in the Olduvai Gorge, Tanganyika, is 600,000 years old, and represents the "missing link" between the South African "ape men" and true men. He gave the news at the Fourth Pan-African Congress of Pre-history at Leopoldville, and said that when all the fragments have been fitted together the skull will eventually go to the British Museum.

COMING EVENTS

British Tuberculosis Association and Yorkshire Thoracic Society.—The provincial meeting of the Association in collaboration with the Yorkshire Thoracic Society will be held in Leeds on September 25 and 26. Details from the Secretary of the Association, 59, Portland Place, London, W.1. (MUS 3810.)

Birmingham Medical Institute.—The annual dinner of the Psychiatry Section will be held on October 2 at the Birmingham Medical Institute, Edgbaston, at 7.30 p.m. Sir GEOFFREY VICKERS will be the guest of honour. Details from the Secretary of the Institute, 36, Harborne Road, Birmingham, 15.

Joint Meeting of the Associations of Clinical Pathologists and of Clinical Biochemists.—Symposia on thyroid antibodies and on newer aspects of enzymes in clinical chemistry will be held on October 3 at the Royal College of Surgeons, starting at 9.30 a.m. Details from Dr. A. B. ANDERSON, Department of Pathology, St. Bartholomew's Hospital, London, E.C.1.

Chartered Society of Physiotherapy.—Annual general meeting, and Founders' Lecture, "The Treatment of Peripheral Paralysis," delivered by Mr. H. J. SEDDON, October 3, 2.30 to 5 p.m., Great Hall, B.M.A. House, Tavistock Square, London, W.C.1.

Sir Charles Hastings Festival.—This Festival will be held at Worcester on October 14. Sir ZACHARY COPE will deliver the memorial oration.

Royal Northern Hospital: Annual Clinical Exhibition.—This will be held in the Board Room during the week commencing October 19, and all practitioners are invited to attend. Exhibits will be on view from 9 a.m. to 9 p.m., with a film show at 8.30 p.m., followed by refreshments.

Manchester Occupational Health Course.—Details of the postgraduate course in occupational health to be held at the Nuffield Department of Occupational Health, Manchester, November 2–7, should be obtained from the Secretary, Department of Occupational Health, Manchester University, Manchester, 13, and not from the London School of Hygiene and Tropical Medicine.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Annals of the Rheumatic Diseases.—Issued quarterly (£3 annually). The new issue (Vol. 18, No. 2) includes:

TREATMENT OF RHEUMATOID ARTHRITIS BY A SANATORIUM REGIME. R. M. Mason and W. G. Wenley.
CORTICOTROPHIN (ACTH) IN RHEUMATOID ARTHRITIS. O. Savage, P. S. Davis, L. Chapman, J. Wickings, J. D. Robertson, and W. S. C. Copeman.
LESIONS OF JOINTS AND TENDON SHEATHS IN SYSTEMIC LUPUS ERYTHEMATOSUS. Bruce Cruickshank.
TRIALS OF CORTISONE ANALOGUES IN THE TREATMENT OF RHEUMATOID ARTHRITIS. H. W. Fladee, G. R. Newns, W. D. Smith, and H. F. West.
METABOLISM OF CONNECTIVE TISSUE IN LIMB ATROPHY IN THE RABBIT. James W. Brooke and H. G. Bewick Slack.
EFFECT OF ASPIRIN ON CUTANEOUS RESPONSE TO THE LOCAL APPLICATION OF AN ESTER OF NICOTINIC ACID. Leslie H. Truelove and J. J. R. Duthie.
EMPIRE RHEUMATISM COUNCIL. TWENTY-SECOND ANNUAL REPORT.
HEBERDEN SOCIETY.
B.M.A. JOINT ANNUAL MEETING WITH C.M.A.
CANADIAN RHEUMATISM ASSOCIATION.
ARGENTINE LEAGUE AGAINST RHEUMATISM.
EUROPEAN LEAGUE AGAINST RHEUMATISM.
TURKISH ASSOCIATION FOR RHEUMATISM RESEARCH AND TREATMENT.
BRITISH RHEUMATIC ASSOCIATION.
NEW YORK RHEUMATISM ASSOCIATION.
ABSTRACTS.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, September 18

BIOCHEMICAL SOCIETY.—At Department of Biological Chemistry, Marischal College, Aberdeen University, 11.30 a.m., 387th meeting.
BRITISH INSTITUTE OF RADIOLOGY.—2.15 p.m., Radiobiology meeting. Short papers by Dr. W. M. Court Brown, Dr. B. Jolles and Miss M. Remington, Dr. R. H. Mole, Dr. N. M. Blackett, Mr. J. T. Lett, Dr. K. A. Stacey and Dr. P. Alexander, and Dr. Margery G. Ord and Dr. L. A. Stocken.

Saturday, September 19

KENT PAEDIATRIC AND CHILD HEALTH SOCIETY.—At Children's Department, Farnborough Hospital, Kent, 3 p.m., Dr. Guy Mitchell: Some Aspects of Separation Experiences in Childhood.
NUTRITION SOCIETY.—At Department of Biological Chemistry, Marischal College, Aberdeen University, 1.45 p.m., 127th meeting. Symposium: Nutrition at the Cellular Level.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Maclure.—On August 5, 1959, at Lincoln, to Dr. Nancy Maclure (formerly Macfarlane), wife of Dr. Alastair Maclure, a son—Fraser Fortay.
Tweedie.—On May 26, 1959, at Liverpool Maternity Hospital, to Joyce (formerly Watkin), M.B., Ch.B., D.P.H., and Kenneth Tweedie, M.Sc., A.Inst.P., a daughter—Clare Margaret.

MARRIAGES

Warwick-Duncan.—On August 30, 1959, at St. Paul's Church, Penn Road, Wolverhampton, Dr. W. J. G. Warwick to Mrs. Iris Duncan.

DEATHS

Aveling.—On August 10, 1959, at Stanborough's Nursing Home, Garston, Herts, Kenneth John Aveling, M.B., B.S., of Watford, Herts.
Blunt.—On August 2, 1959, at Bournemouth, Hants, Arthur Leslie Blunt, M.R.C.S., L.R.C.P.
Bradford.—On July 15, 1959, Richard Avenel Bradford, M.R.C.S., L.R.C.P., of Oakhill Avenue, Hampstead, London, N.W.
Bryant.—On July 13, 1959, at Auckland, New Zealand, Ernest Horace Bryant, L.R.C.P., M.R.C.S., L.D.S., formerly of Tunbridge Wells, Kent.
Caldwell-Smith.—On July 16, 1959, at 42, Somerset Road, London, S.W., Eric Lauder Caldwell-Smith, O.B.E., M.B., B.Ch.
Cooper.—On July 24, 1959, John Sephton Cooper, M.B., B.Ch., of 12, Hurle Crescent, Clifton, Bristol, formerly of Clitheroe, Lancs, aged 81.
Coulson.—On July 11, 1959, Thomas Edmund Coulson, M.D., F.R.C.S.Ed., of Balsam Gate, Wincanton, Somerset.
Craig.—On July 30, 1959, Robert Craig, M.B., Ch.B., late of Oldfield Park, Bath, Somerset.
Davies.—On August 7, 1959, at Shrewsbury, Salop, David William Davies, M.R.C.S., L.R.C.P., D.P.H., Major, R.A.M.C.
Dodd.—On July 31, 1959, at Hove, Sussex, Herbert Grantham Dodd, T.D., M.B., B.S., F.F.A. R.C.S., Major, R.A.M.C., retired.
Ellis.—On August 9, 1959, at Boscombe Hospital, Hants, Dudley Anton Millard Ellis, M.B., B.S., M.R.C.P., of 17, Queen's Park Avenue, Bournemouth, Hants, late of Oakwood Avenue, Beckenham, Kent, aged 29.
Falwasser.—On July 11, 1959, Arthur Thomas Falwasser, D.S.O., M.R.C.S., L.R.C.P., of West Malling, Kent, aged 85.
Farebrother.—On July 30, 1959, at his home, 33, Colneis Road, Felixstowe, Suffolk, Harold William Farebrother, M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., retired.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Circumcision

Q.—*What are the latest views on the need for circumcision for phimosis in infants ?*

A.—Opinion on the need for neonatal circumcision has changed radically in the past fifteen years. Before the war circumcision was carried out on the majority of male infants, especially in the higher social classes. Now it is the minority who suffer this operation for other than ritual purposes. Fashion and the swing of the pendulum may be responsible, therefore, for both the previous and the present position. Gairdner[1] had a great deal to do with influencing opinion against routine circumcision, and his paper on this subject is still unexcelled. He showed that the prepuce was naturally adherent to the glans penis in most infants at birth and that the epithelial cells which caused this fusion gradually disappeared during the first year of life. Hence the foreskin becomes retractile by a normal process of development. Forcible stretching and retraction of the foreskin is therefore contraindicated and circumcision normally not necessary, since retractability of the foreskin is likely to occur in most cases. However, it is not possible to forecast in which infants failure to retract and phimosis may persist. All that can be said is that this occurs in very few.

Gairdner pointed out that meatal ulcers are found in the circumcised infant and not in the uncircumcised, and emphasized the amount of trouble they were apt to cause. He also noted that scarring and damage from ill-performed operations was seen from time to time. He gave the following table of deaths as a result of circumcision (taken from the Registrar-General's returns under the heading of circumcision and phimosis).

	0–1 Yr.	1–5 Yrs.
1942	12	4
1943	10	7
1944	10	6
1945	15	2
1946	16	3
1947	9	1

The mortality in subsequent years (Registrar-General's returns under the heading of redundant prepuce and phimosis) is as follows:

	Years				
	0–	1–	2–	3–	4–
1957	1	—	—	—	—
1956	3	—	—	—	—
1955	1	—	—	—	—
1954	—	—	—	—	—
1953	—	—	—	—	—
1952	4	2	—	—	—
1951	1	—	—	—	—
1950	6	—	—	—	—

There has been, therefore, an apparent saving, since circumcision has been more selectively performed, of some 10 to 15 lives a year of children under the age of 5. Circumcision in infancy, of course, excludes the possibility of trouble in the future from paraphimosis and balanitis, which are, however, avoidable without circumcision. It also removes the possibility that circumcision may need to be performed later on account of phimosis, with all the troublesome consequences of such an operation on a small boy or those of older age. Also in favour of routine circumcision are two unquestioned facts—the decreased incidence of carcinoma of the penis in the circumcised, and of carcinoma of the cervix in wives of circumcised as compared with those of uncircumcised males. It is of course possible to argue that hygiene rather than circumcision is the better means of preventing these conditions.

In considering the individual case it is necessary to weigh the disadvantages of an operation which carries a risk of a very small but definite mortality, and a minor risk of a possible meatal ulcer, against the advantages of freedom from the risks of phimosis, paraphimosis, and balanitis in the immediate future and of carcinoma of the penis in the more distant future. The choice must be a matter of individual opinion, influenced by any decided parental preference, but always weighted by the fact that if anything were to go wrong it would not be possible to maintain to oneself that the operation was essential.

REFERENCE

[1] Gairdner, D., *Brit. med. J.*, 1949, **2**, 1433.

Cervical Disk Lesion

Q.—*What is the treatment for and prognosis in a cervical disk lesion which is causing neuritic symptoms in the right arm ?*

A.—A cervical disk lesion is very commonly an osteoarthritic protuberance into the nerve root foramen, usually from the joint between the bodies but sometimes from the joints of Luschka. In a number, however, true disk prolapse occurs and may easily cause cord pressure symptoms rather than nerve root changes.

The difference in pathology between the lumbar and cervical regions is important in that the cervical vertebral changes are likely to be more permanent, though not necessarily with symptoms. Cervical disk lesions causing neuritic symptoms in the arm will frequently recover quickly with neck traction. If this fails a plaster or cardboard collar is the next effective measure which should be tried. If pain is really serious and unrelieved by the above methods, bed rest with skull traction with a Blackburn calliper is necessary.

It is only when these methods have failed, or if there is serious pain and paralysis which has not recovered, that surgical exploration for a cervical disk is undertaken. The operation is much more difficult and hazardous than in the lumbar region, and is in fact most commonly undertaken because of cord pressure. Chronic symptoms not responding to the above measures may occasionally need a localized fusion of cervical vertebrae, which is often undertaken by an antero-lateral approach.

Foot-drop

Q.—*What are the rarer causes of foot-drop ?*

A.—Foot-drop may be caused by disease of the anterior tibial group of muscles or by disorder of the lower motor neurone which innervates these muscles. A spastic foot-drop may occur with any upper motor neurone lesion which affects the leg. The pathological lesions which may cause foot-drop range in location from a parasagittal lesion, such as a neoplasm, to a primary muscle disease such as dystrophia myotonica. The frequency or rarity of the disorder causing foot-drop will presumably vary with the type of clinical material being seen.

Aplastic Anaemia due to Chloramphenicol

Q.—*(1) What is the prognosis in aplastic or hypoplastic anaemia associated with a history of taking chloramphenicol ? (2) What is the treatment ? (3) What is the value of cobalt chloride in treatment ?*

A.—Aplastic or hypoplastic anaemia associated with the taking of chloramphenicol is a serious event, and many patients have died as a result. The outlook is, however, probably less grave than in aplastic anaemia of unknown origin, and recovery is possible. Treatment can be only palliative and expectant. Transfusions of whole blood should be given as required, and there is a theoretical advantage at least in using blood which has been freshly

collected in plastic equipment so that viable platelets may be transfused. Antibiotics should be reserved to treat sepsis if and when this develops. Adrenal steroids have often been given, but it is uncertain whether they are of real value. Cobalt chloride is probably of no value in treatment.

Ethylene Disulphonate in Asthma

Q.—*What is the rationale of the treatment of asthma by injections of ethylene disulphonate? Are there any serious contraindications to its use?*

A.—The use of ethylene disulphonate in asthma was first advocated by Evans, Bodman, and Maisin,[1] who set out the rationale in detail. Briefly, it was based on the idea that the absence of certain catalysts of co-enzyme activity was the primary cause of allergic manifestations. Support for this was based on a degree of protection obtained in anaphylactic guinea-pigs, and four clinical cases were described. Ethylene disulphonate was marketed as "allergosil." The solution was rapidly oxidized by air, and special syringes, specially cleaned and sterilized, were necessary. In chronic cases of asthma it was advised that the following preliminary preparation was necessary: (1) removal of intestinal toxaemia; (2) withholding certain drugs, including alcohol, barbiturates, and tobacco; and (3) special dieting, excluding meat and adding extra vitamins, and nikethamide by mouth. The injections were temporarily painful and "faintness" might occur.

The treatment received national publicity in the United States[2 3] and Fish *et al.*[4] therefore reinvestigated its effect on the prevention of anaphylaxis in animals, the basis on which the treatment was given in man. They failed to find that it gave protection. Although some clinical reports were favourable,[5–7] others could not confirm the clinical claims.[8 9] There is therefore considerable doubt about its value. The writer has been unable to trace the original manufacturers, and allergosil is apparently unavailable now.

REFERENCES

1 Evans, G., Bodman, J., and Maisin, J. H., *Med. Press*, 1940, **203**, 457 and 476.
2 *J. Amer. med. Ass.*, 1942, **120**, 842.
3 *Newsweek*, October 12, 1952, as quoted in reference 2.
4 Fish, R. T., Small, W. S., and Foord, A. G., *J. Allergy*, 1944, **15**, 14.
5 Smith, N. M., *Clin. Med.*, 1944, **51**, 323.
6 Wasson, V. P., *Arch. Pediat.*, 1943, **60**, 511.
7 Bartlett, C. L., ibid., 1944, **61**, 311.
8 Archibald, H. C., ibid., 1945, **62**, 219.
9 Kurland, L. T., and Bubert, H. M., *Bull. Sch. Med. Maryland*, 1945, **30**, 46.

Urinary Retention in Tabes

Q.—*What is the treatment for a patient with urinary retention due to tabes dorsalis?*

A.—Initial treatment consists of catheterization and bladder drainage for a week or so. At the end of this time a trial of micturition is made; the catheter is removed and the male patient is instructed to attempt to pass water in a sitting position, using his accessory muscles and pressing the abdomen with his hands. If this manœuvre is unsuccessful drainage by catheter is continued for a further seven to ten days, when a second trial of micturition is made. If the second trial of micturition fails the next step is usually a surgical resection of the bladder neck. This operation is highly effective. Careful post-operative treatment and follow-up are necessary. Needless to say, urinary infection should be treated and precautions taken to avoid introduction of infection into the bladder at catheterization.

Repetition of A.T.S.

Q.—*What treatment should be given to a patient with a contaminated wound who has been given A.T.S. previously and who has not been actively immunized?*

A.—The risk of death from unmodified tetanus is high. The risk of death from an anaphylactic reaction after A.T.S. is, by comparison, very low. There seems no doubt, therefore, that in the circumstances quoted A.T.S. must be given. The usual dosage is 1,500 units, and in most cases there is no need to give more or to repeat the dose. In the present case the previous administration of A.T.S. may have rendered the patient sensitive to horse serum, with the result that the elimination of the antitoxin is greatly speeded up and may be complete in 2 to 3 days. Two courses are open—either to give double or treble the dose or to give a dose of 1,500 units twice more at weekly intervals. There is no guarantee that increasing the dose in a sensitive patient will lead to longer protection. On the other hand, repeating the dose will certainly increase the risk of severe reactions. Either course would be regarded as reasonable from medical and legal angles. Since the patient seems subject to the risk of contaminated wounds, he should most certainly be offered active immunization six weeks after the last dose of antitoxin.

Criminal Abortion

Q.—*Is disease in the foetus an acceptable defence in law to a charge of criminal abortion?*

A.—It is a defence to a charge of abortion that the pregnancy is terminated with the bona-fide object of preserving the mother's life or preserving her physical or mental health from ruin. Foetal health can be relevant only if it is necessary to remove the foetus for the sake of the mother. There seem to be no reported cases in which considerations of foetal health alone have been put forward by way of defence.

NOTES AND COMMENTS

Thumb-sucking.—Mr. GEOFFREY H. SPERBER (London, W.C.1) writes: It is with considerable surprise that I note your contributor of the answer to the question on thumb-sucking ("Any Questions?" July 4, p. 25) advocating "sucking or chewing sweets" as a means of overcoming the thumb-sucking habit. Few factors could be more detrimental to the dentition, and nothing more cariogenic. Having established the thumb-sucking to be a habit only—that is, having no emotional significance—the best method of deterring the child from putting the thumb in the mouth, after appealing to the child's common sense, to which it is often responsive, is to make the thumb a distasteful object to suck. This will quickly lead to the breaking of the habit. Means of making the thumb distasteful are many, but one of the simplest is the wearing of a glove on the hand habitually sucked. A co-operative child will not pull off the glove, but will see it as an aid to its breaking the habit. Another method, less obvious to onlookers, and useful in the slightly less co-operative child, is to paint the thumb with tincture of bitter aloes, whose disagreeable taste will quickly draw the child's attention to the fact that its thumb is in its mouth. Any encouragement of the usually excessive sweet-eating in the children of to-day is to be greatly deprecated.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Emergencies in General Practice (26s. 9d.).

Refresher Course for General Practitioners, Volumes 2 and 3 (26s. 9d. each).

Clinical Pathology in General Practice (22s. 3d.).

Any Questions?, Volumes 2 and 3 (8s. 3d. each).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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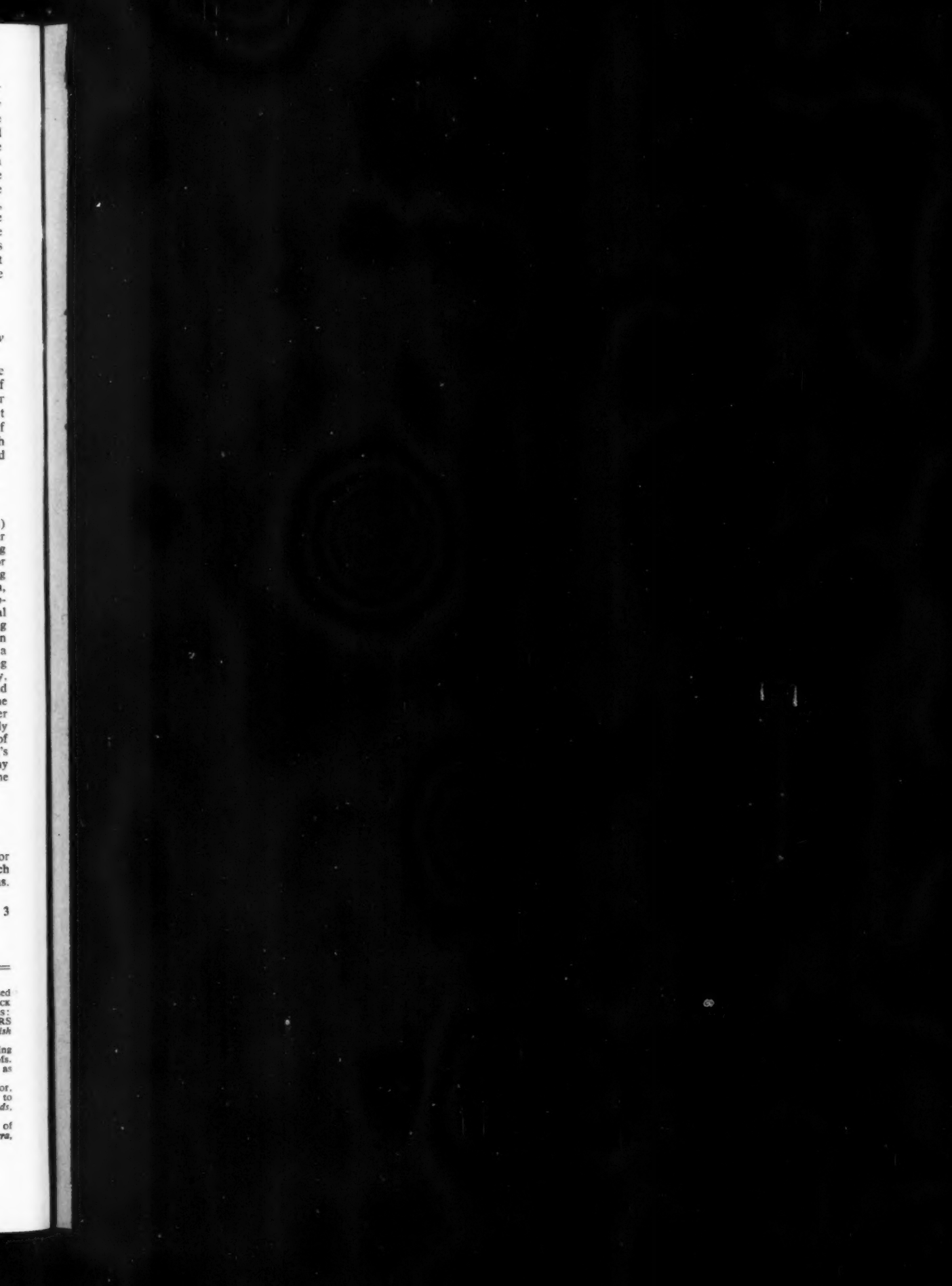
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